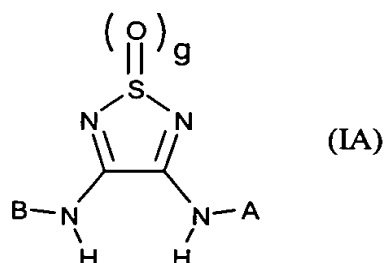


WHAT IS CLAIMED IS:

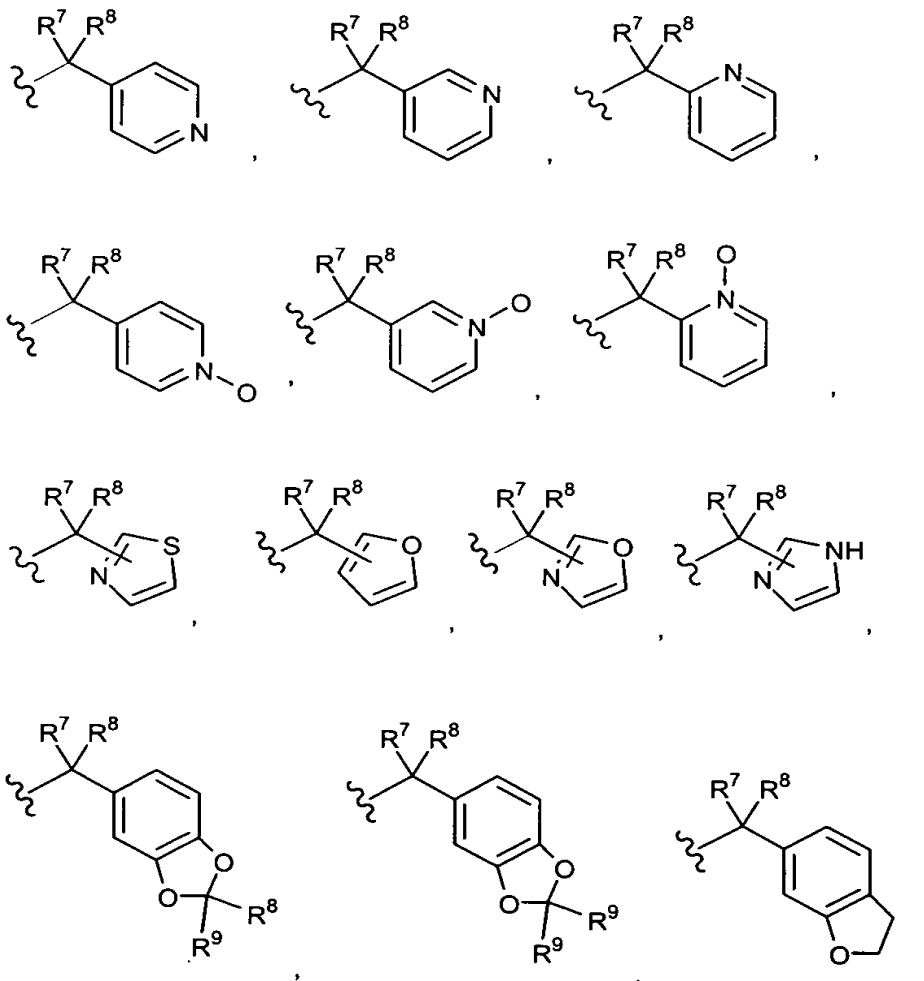
1. A compound of the formula:



- 5 and the pharmaceutically acceptable salts and solvates thereof, wherein:

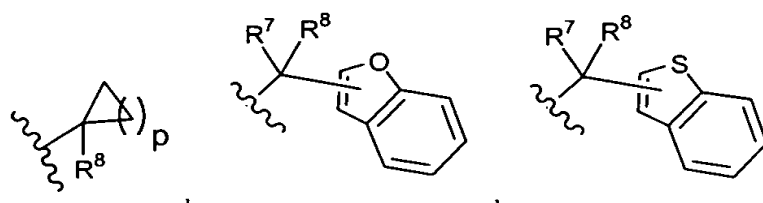
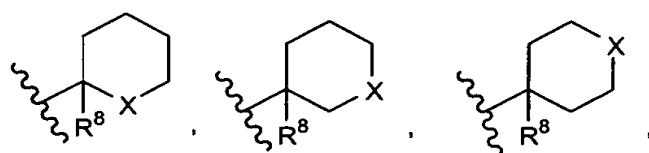
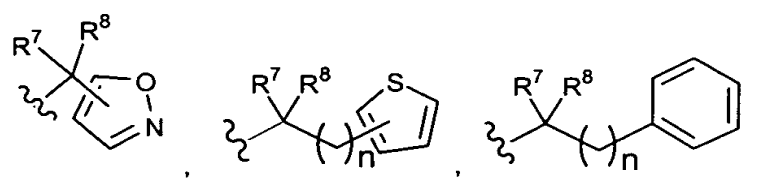
A is selected from the group consisting of:

(1)

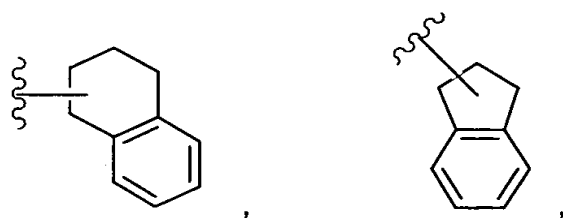
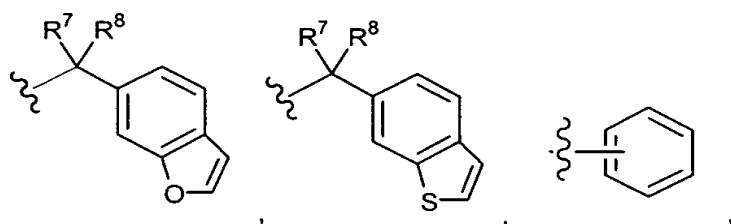


10

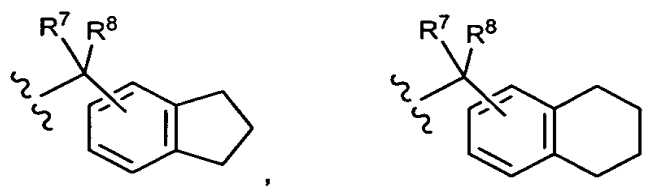
15

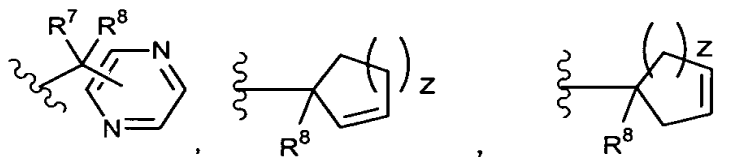
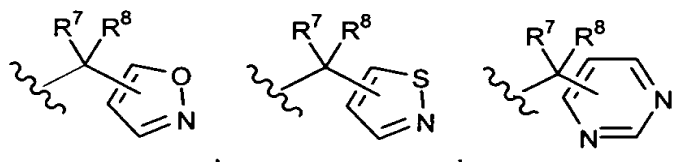
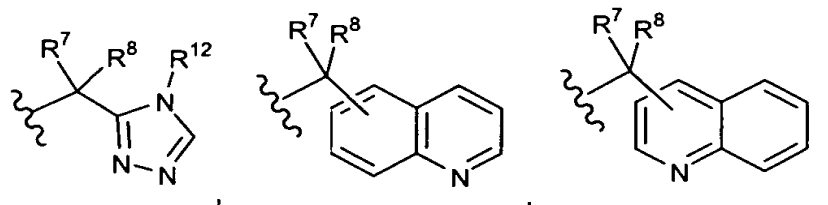


5

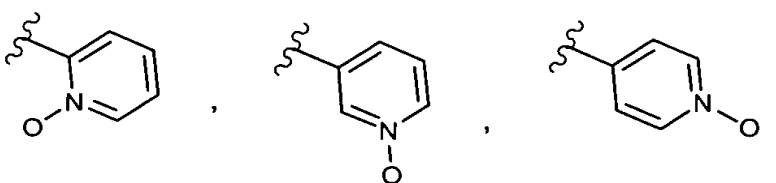
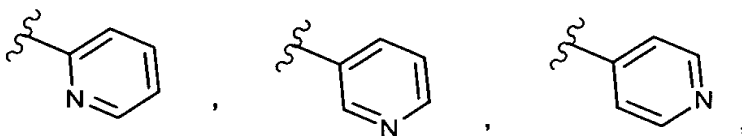


10

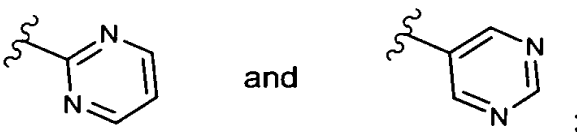




5

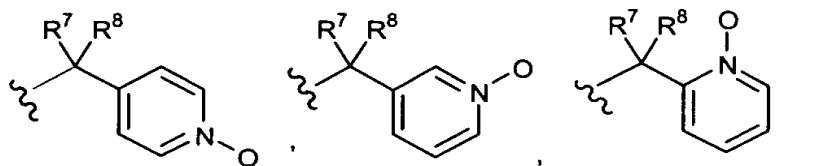
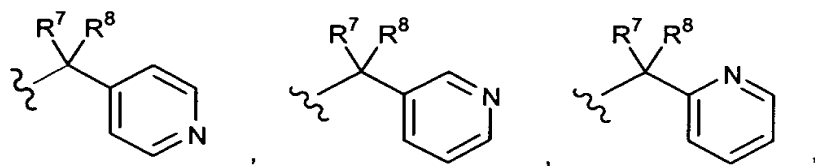


10

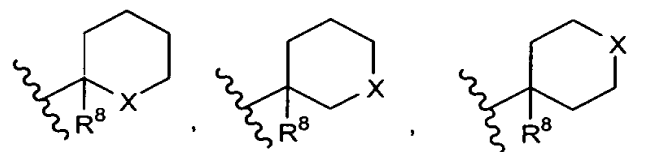
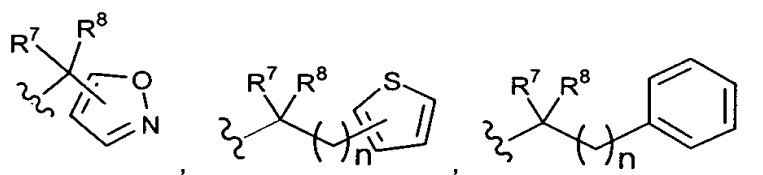
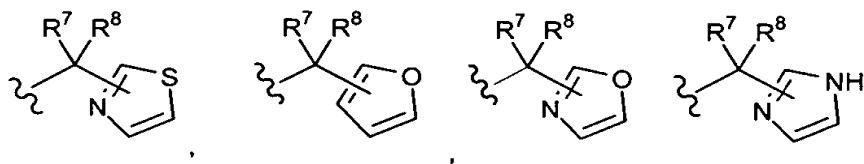


15

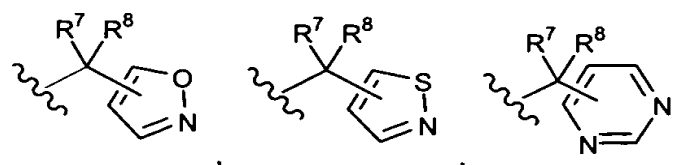
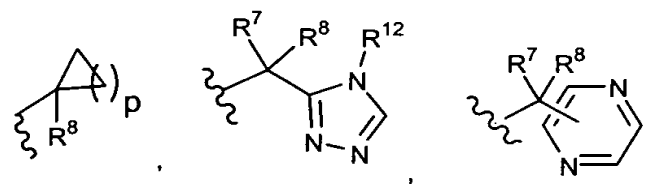
(2)



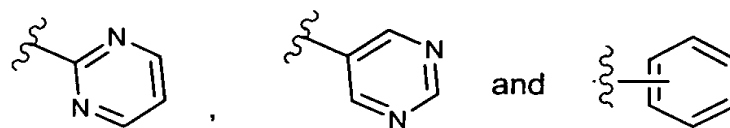
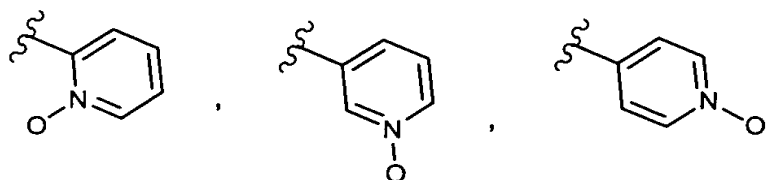
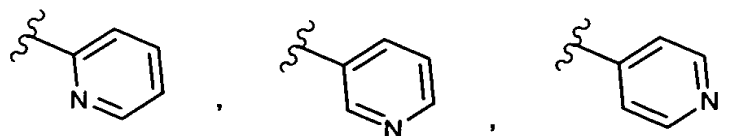
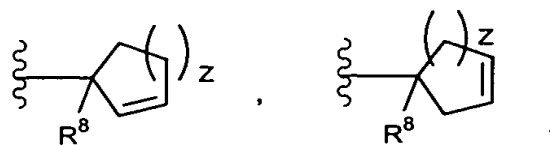
5



10



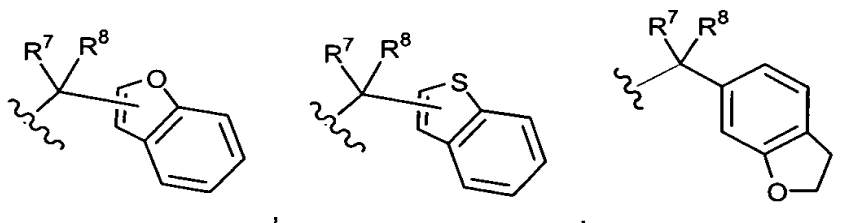
15



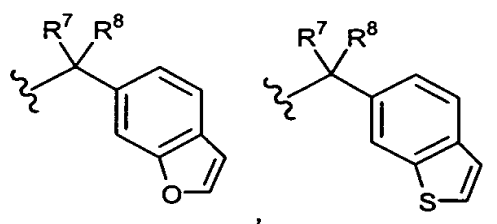
5

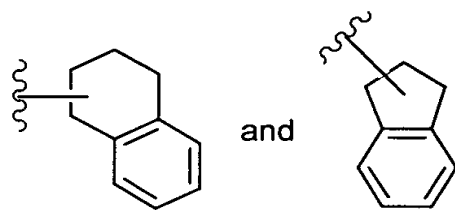
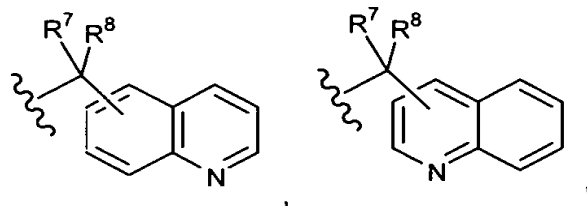
wherein the above rings of said A groups are substituted with 1 to 6  
 10 substituents each independently selected from the group consisting of: R<sup>9</sup> groups;

(3)

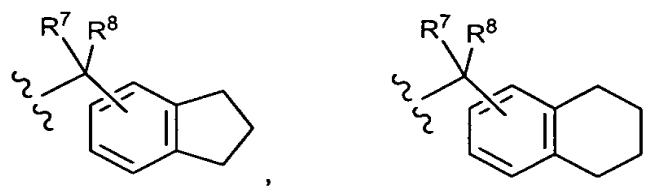


15





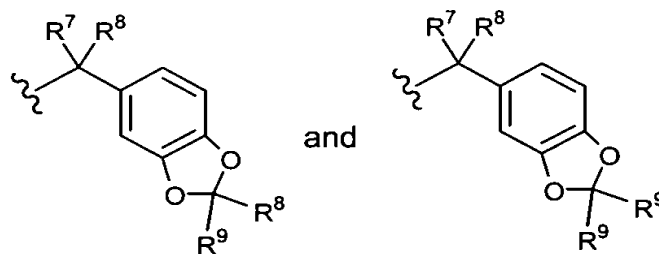
5



wherein one or both of the above rings of said A groups are substituted with 1 to 6 substituents each independently selected from the group consisting of:  $R^9$  groups;

10

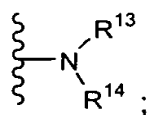
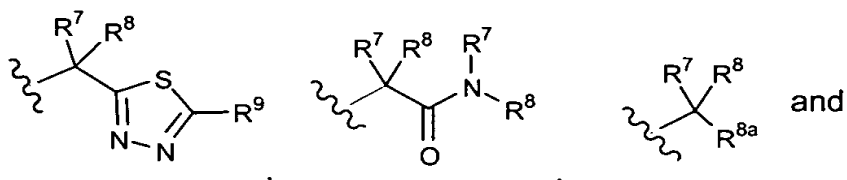
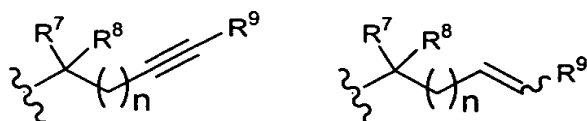
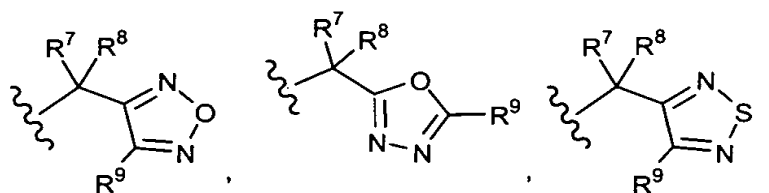
(4)



15

wherein the above phenyl rings of said A groups are substituted with 1 to 3 substituents each independently selected from the group consisting of:  $R^9$  groups; and

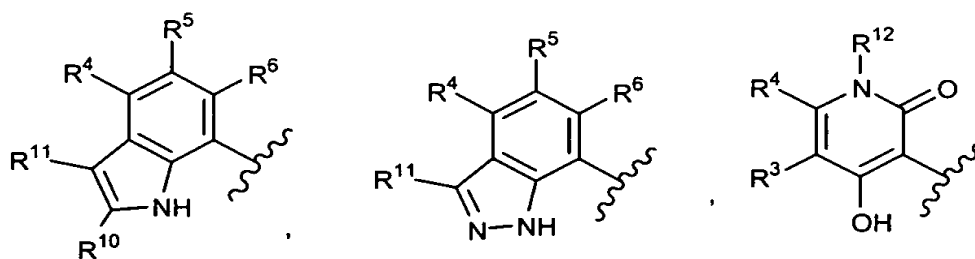
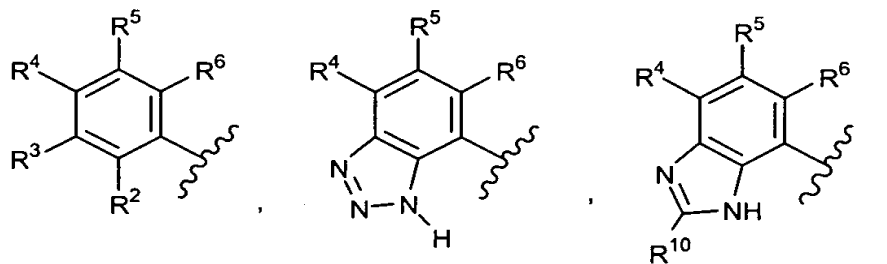
(5)

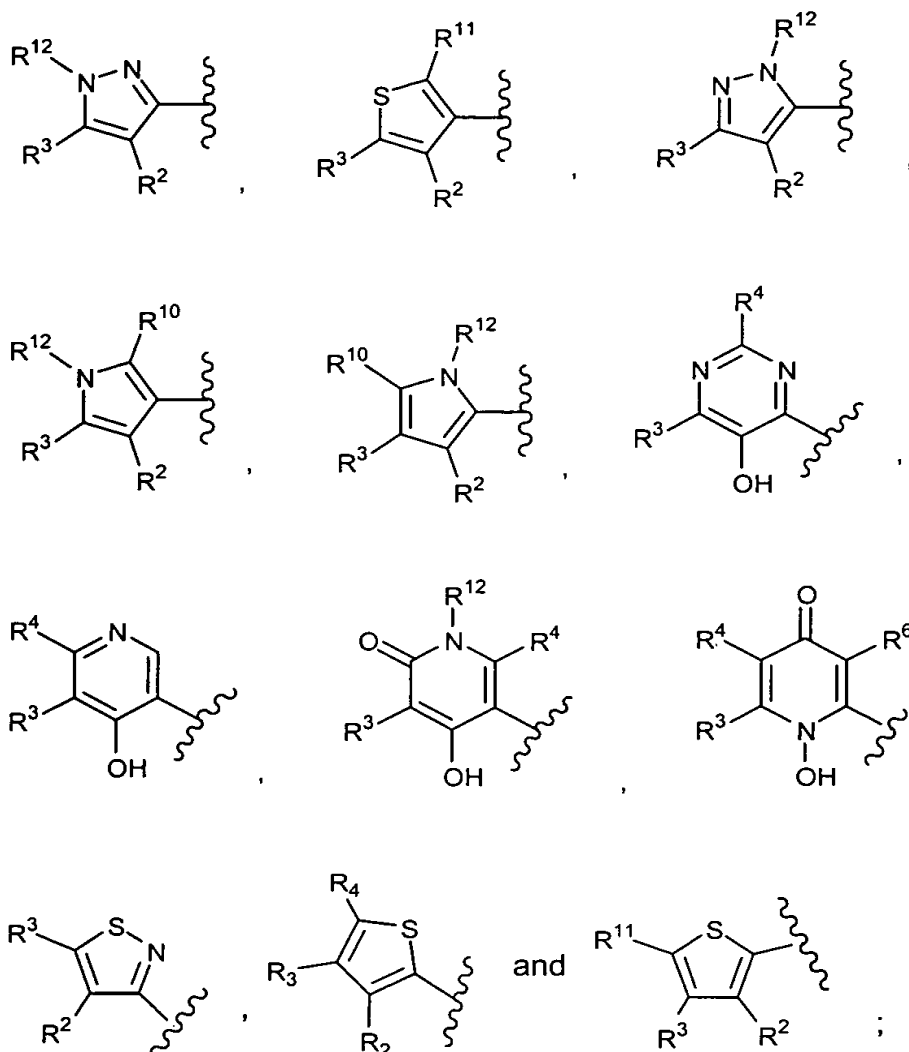


5

10

B is selected from the group consisting of





n is 0 to 6;

p is 1 to 5;

X is O,  $\text{NR}^{18}$ , or S;

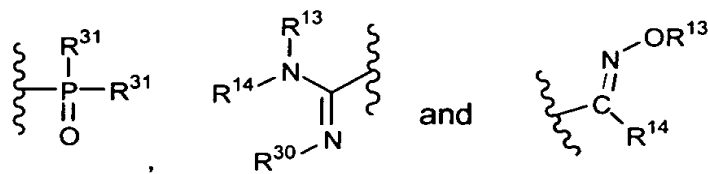
Z is 1 to 3;

$R^2$  is selected from the group consisting of: hydrogen, OH,  $-\text{C}(\text{O})\text{OH}$ ,  $-\text{SH}$ ,  $-\text{SO}_2\text{NR}^{13}\text{R}^{14}$ ,  $-\text{NHC}(\text{O})\text{R}^{13}$ ,  $-\text{NHSO}_2\text{NR}^{13}\text{R}^{14}$ ,  $-\text{NHSO}_2\text{R}^{13}$ ,  $-\text{NR}^{13}\text{R}^{14}$ ,  $-\text{C}(\text{O})\text{NR}^{13}\text{R}^{14}$ ,  $-\text{C}(\text{O})\text{NHOR}^{13}$ ,  $-\text{C}(\text{O})\text{NR}^{13}\text{OH}$ ,  $-\text{S}(\text{O}_2)\text{OH}$ ,  $-\text{OC}(\text{O})\text{R}^{13}$ , an unsubstituted heterocyclic acidic functional group, and a substituted heterocyclic acidic functional group; wherein

there are 1 to 6 substituents on said substituted heterocyclic acidic functional group each substituent being independently selected from the group consisting of:  $R^9$  groups;

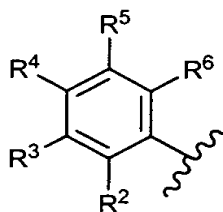


each  $R^3$  and  $R^4$  is independently selected from the group consisting of:  
hydrogen, cyano, halogen, alkyl, alkoxy, cycloalkyl substituted with 1 to 4 alkyl groups  
wherein each alkyl group is independently selected, unsubstituted cycloalkyl,  
cycloalkyl substituted with 1 to 4 alkyl groups,  $-OH$ ,  $-CF_3$ ,  $-OCF_3$ ,  $-NO_2$ ,  $-C(O)R^{13}$ ,  
5  $-C(O)OR^{13}$ ,  $-C(O)NHR^{17}$ ,  $-C(O)NR^{13}R^{14}$ ,  $-SO_{(t)}NR^{13}R^{14}$ ,  $-SO_{(t)}R^{13}$ ,  $-C(O)NR^{13}OR^{14}$ ,  
unsubstituted or substituted aryl, unsubstituted or substituted heteroaryl,

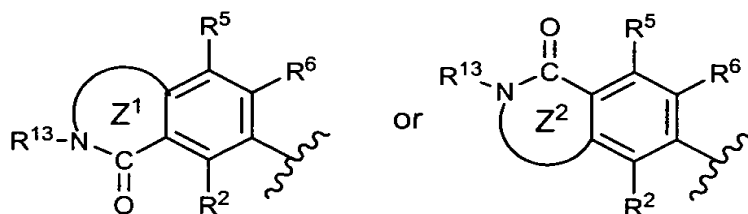


wherein there are 1 to 6 substituents on said substituted aryl group and each  
substituent is independently selected from the group consisting of:  $R^9$  groups; and  
10 wherein there are 1 to 6 substituents on said substituted heteroaryl group and each  
substituent is independently selected from the group consisting of:  $R^9$  groups; or

$R^3$  is and  $R^4$  taken together with the carbons atoms to which they are bonded  
to in the the phenyl B substituent



15 form a fused ring of the formula:



wherein  $Z^1$  or  $Z^2$  is an unsubstituted or substituted saturated heterocyclic ring  
(preferably a 4 to 7 membered heterocyclic ring), said ring  $Z^1$  or  $Z^2$  optionally  
containing one additional heteroatom selected from the group consisting of: O, S and  
20  $NR^{18}$ ; wherein there are 1 to 3 substituents on said ring  $Z^1$  or  $Z^2$ , and each substituent  
is independently selected from the group consisting of: alkyl, aryl, hydroxy,  
hydroxyalkyl, alkoxy, alkoxyalkyl, arylalkyl, fluoroalkyl, cycloalkyl, cycloalkylalkyl,  
heteroaryl, heteroarylalkyl, amino,  $-C(O)OR^{15}$ ,  $-C(O)NR^{15}R^{16}$ ,  $-SO_tNR^{15}R^{16}$ ,  $-C(O)R^{15}$ ,

$-\text{SO}_2\text{R}^{15}$  provided that  $\text{R}^{15}$  is not H,  $-\text{NHC}(\text{O})\text{NR}^{15}\text{R}^{16}$ ,  $-\text{NHC}(\text{O})\text{OR}^{15}$ , halogen, and a heterocycloalkenyl group;

each  $\text{R}^5$  and  $\text{R}^6$  are the same or different and are independently selected from the group consisting of hydrogen, halogen, alkyl, alkoxy,  $-\text{CF}_3$ ,  $-\text{OCF}_3$ ,

5  $-\text{NO}_2$ ,  $-\text{C}(\text{O})\text{R}^{13}$ ,  $-\text{C}(\text{O})\text{OR}^{13}$ ,  $-\text{C}(\text{O})\text{NR}^{13}\text{R}^{14}$ ,  $-\text{SO}_2\text{NR}^{13}\text{R}^{14}$ ,  $-\text{C}(\text{O})\text{NR}^{13}\text{OR}^{14}$ , cyano, unsubstituted or substituted aryl, and unsubstituted or substituted heteroaryl group; wherein there are 1 to 6 substituents on said substituted aryl group and each substituent is independently selected from the group consisting of:  $\text{R}^9$  groups; and wherein there are 1 to 6 substituents on said substituted heteroaryl group and each substituent is independently selected from the group consisting of:  $\text{R}^9$  groups;

10 each  $\text{R}^7$  and  $\text{R}^8$  is independently selected from the group consisting of: H, unsubstituted or substituted alkyl, unsubstituted or substituted aryl, unsubstituted or substituted heteroaryl, unsubstituted or substituted arylalkyl, unsubstituted or substituted heteroarylalkyl, unsubstituted or substituted cycloalkyl, unsubstituted or substituted cycloalkylalkyl,  $-\text{CO}_2\text{R}^{13}$ ,  $-\text{CONR}^{13}\text{R}^{14}$ , alkynyl, alkenyl, and cycloalkenyl; and wherein there are one or more substituents on said substituted  $\text{R}^7$  and  $\text{R}^8$  groups, wherein each substituent is independently selected from the group consisting of:

- a) halogen,
- b)  $-\text{CF}_3$ ,
- 20 c)  $-\text{COR}^{13}$ ,
- d)  $-\text{OR}^{13}$ ,
- e)  $-\text{NR}^{13}\text{R}^{14}$ ,
- f)  $-\text{NO}_2$ ,
- g)  $-\text{CN}$ ,
- 25 h)  $-\text{SO}_2\text{OR}^{13}$ ,
- i)  $-\text{Si}(\text{alkyl})_3$ , wherein each alkyl is independently selected,
- j)  $-\text{Si}(\text{aryl})_3$ , wherein each alkyl is independently selected,
- k)  $-(\text{R}^{13})_2\text{R}^{14}\text{Si}$ , wherein each  $\text{R}^{13}$  is independently selected,
- l)  $-\text{CO}_2\text{R}^{13}$ ,
- 30 m)  $-\text{C}(\text{O})\text{NR}^{13}\text{R}^{14}$ ,
- n)  $-\text{SO}_2\text{NR}^{13}\text{R}^{14}$ ,
- o)  $-\text{SO}_2\text{R}^{13}$ ,
- p)  $-\text{OC}(\text{O})\text{R}^{13}$ ,
- q)  $-\text{OC}(\text{O})\text{NR}^{13}\text{R}^{14}$ ,

r)  $-\text{NR}^{13}\text{C}(\text{O})\text{R}^{14}$ , and

s)  $-\text{NR}^{13}\text{CO}_2\text{R}^{14}$ ;

(fluoroalkyl is one non-limiting example of an alkyl group that is substituted with halogen);

5  $\text{R}^{8a}$  is selected from the group consisting of: hydrogen, alkyl, cycloalkyl and cycloalkylalkyl;

each  $\text{R}^9$  is independently selected from the group consisting of:

a)  $-\text{R}^{13}$ ,

b) halogen,

10 c)  $-\text{CF}_3$ ,

d)  $-\text{COR}^{13}$ ,

e)  $-\text{OR}^{13}$ ,

f)  $-\text{NR}^{13}\text{R}^{14}$ ,

g)  $-\text{NO}_2$ ,

15 h)  $-\text{CN}$ ,

i)  $-\text{SO}_2\text{R}^{13}$ ,

j)  $-\text{SO}_2\text{NR}^{13}\text{R}^{14}$ ,

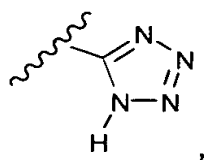
k)  $-\text{NR}^{13}\text{COR}^{14}$ ,

l)  $-\text{CONR}^{13}\text{R}^{14}$ ,

20 m)  $-\text{NR}^{13}\text{CO}_2\text{R}^{14}$ ,

n)  $-\text{CO}_2\text{R}^{13}$ ,

o)



p) alkyl substituted with one or more  $-\text{OH}$  groups,

25 q) alkyl substituted with one or more  $-\text{NR}^{13}\text{R}^{14}$  group, and

r)  $-\text{N}(\text{R}^{13})\text{SO}_2\text{R}^{14}$ ;

each  $\text{R}^{10}$  and  $\text{R}^{11}$  is independently selected from the group consisting of  $\text{R}^{13}$ , halogen,  $-\text{CF}_3$ ,  $-\text{OCF}_3$ ,  $-\text{NR}^{13}\text{R}^{14}$ ,  $-\text{NR}^{13}\text{C}(\text{O})\text{NR}^{13}\text{R}^{14}$ ,  $-\text{OH}$ ,  $-\text{C}(\text{O})\text{OR}^{13}$ ,  $-\text{SH}$ ,  $-\text{SO}(\text{t})\text{NR}^{13}\text{R}^{14}$ ,  $-\text{SO}_2\text{R}^{13}$ ,  $-\text{NHC}(\text{O})\text{R}^{13}$ ,  $-\text{NHSO}_2\text{NR}^{13}\text{R}^{14}$ ,  $-\text{NHSO}_2\text{R}^{13}$ ,  $-\text{C}(\text{O})\text{NR}^{13}\text{R}^{14}$ ,  $-\text{C}(\text{O})\text{NR}^{13}\text{OR}^{14}$ ,  $-\text{OC}(\text{O})\text{R}^{13}$  and cyano;

30

$R^{12}$  is selected from the group consisting of: hydrogen,  $-C(O)OR^{13}$ , unsubstituted or substituted aryl, unsubstituted or substituted heteroaryl, unsubstituted or substituted arylalkyl, unsubstituted or substituted cycloalkyl, unsubstituted or substituted alkyl, unsubstituted or substituted cycloalkylalkyl, and unsubstituted or substituted heteroarylalkyl group; wherein there are 1 to 6 substituents on the substituted  $R^{12}$  groups and each substituent is independently selected from the group consisting of:  $R^9$  groups;

each  $R^{13}$  and  $R^{14}$  is independently selected from the group consisting of: H, unsubstituted or substituted alkyl, unsubstituted or substituted aryl, unsubstituted or substituted heteroaryl, unsubstituted or substituted arylalkyl, unsubstituted or substituted heteroarylalkyl, unsubstituted or substituted cycloalkyl, unsubstituted or substituted cycloalkylalkyl, unsubstituted or substituted heterocyclic, unsubstituted or substituted fluoroalkyl, and unsubstituted or substituted heterocycloalkylalkyl (wherein "heterocycloalkyl" means heterocyclic); wherein there are 1 to 6 substituents on said substituted  $R^{13}$  and  $R^{14}$  groups and each substituent is independently selected from the group consisting of: alkyl,  $-CF_3$ ,  $-OH$ , alkoxy, aryl, arylalkyl, fluoroalkyl, cycloalkyl, cycloalkylalkyl, heteroaryl, heteroarylalkyl,  $-N(R^{40})_2$ ,  $-C(O)OR^{15}$ ,  $-C(O)NR^{15}R^{16}$ ,  $-S(O)_iNR^{15}R^{16}$ ,  $-C(O)R^{15}$ ,  $-SO_2R^{15}$  provided that  $R^{15}$  is not H, halogen, and  $-NHC(O)NR^{15}R^{16}$ ; or

$R^{13}$  and  $R^{14}$  taken together with the nitrogen they are attached to in the groups  $-C(O)NR^{13}R^{14}$  and  $-SO_2NR^{13}R^{14}$  form an unsubstituted or substituted saturated heterocyclic ring, said ring optionally containing one additional heteroatom selected from the group consisting of: O, S and  $NR^{18}$ ; wherein there are 1 to 3 substituents on the substituted cyclized  $R^{13}$  and  $R^{14}$  groups and each substituent is independently selected from the group consisting of: alkyl, aryl, hydroxy, hydroxyalkyl, alkoxy, alkoxyalkyl, arylalkyl, fluoroalkyl, cycloalkyl, cycloalkylalkyl, heteroaryl, heteroarylalkyl, amino,  $-C(O)OR^{15}$ ,  $-C(O)NR^{15}R^{16}$ ,  $-SO_iNR^{15}R^{16}$ ,  $-C(O)R^{15}$ ,  $-SO_2R^{15}$  provided that  $R^{15}$  is not H,  $-NHC(O)NR^{15}R^{16}$ ,  $-NHC(O)OR^{15}$ , halogen, and a heterocycloalkenyl group;

each  $R^{15}$  and  $R^{16}$  is independently selected from the group consisting of: H, alkyl, aryl, arylalkyl, cycloalkyl and heteroaryl;

$R^{17}$  is selected from the group consisting of:  $-SO_2$ alkyl,  $-SO_2$ aryl,  $-SO_2$ cycloalkyl, and  $-SO_2$ heteroaryl;

$R^{18}$  is selected from the group consisting of: H, alkyl, aryl, heteroaryl,  $-C(O)R^{19}$ ,  $-SO_2R^{19}$  and  $-C(O)NR^{19}R^{20}$ ;

each  $R^{19}$  and  $R^{20}$  is independently selected from the group consisting of: alkyl, aryl and heteroaryl;

$R^{30}$  is selected from the group consisting of: alkyl, cycloalkyl, -CN, -NO<sub>2</sub>, or -SO<sub>2</sub>R<sup>15</sup> provided that R<sup>15</sup> is not H;

5 each  $R^{31}$  is independently selected from the group consisting of: unsubstituted alkyl, unsubstituted or substituted aryl, unsubstituted or substituted heteroaryl and unsubstituted or substituted cycloalkyl; wherein there are 1 to 6 substituents on said substituted  $R^{31}$  groups and each substituent is independently selected from the group consisting of: alkyl, halogen and -CF<sub>3</sub>;

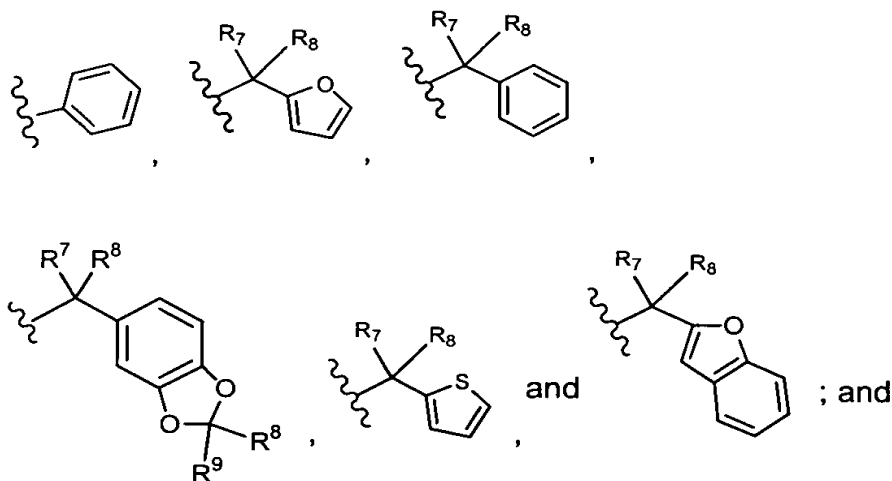
10 each  $R^{40}$  is independently selected from the group consisting of: H, alkyl and cycloalkyl;

g is 1 or 2; and

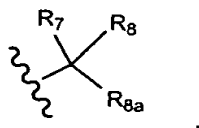
t is 0, 1 or 2.

15 2. The compound of claim 1 wherein A is selected from the group consisting of:

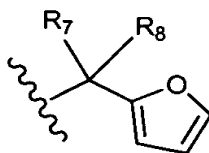
(1) unsubstituted or substituted:



(2)

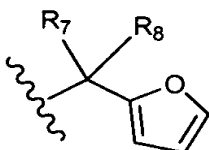


3. The compound of Claim 1 wherein substituent A is:



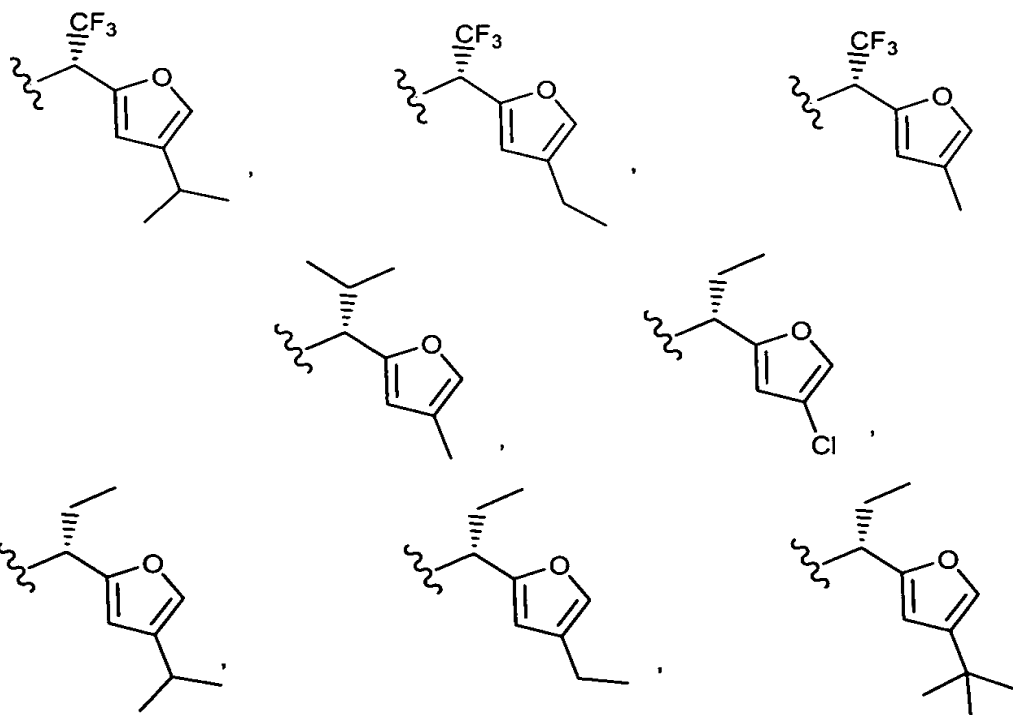
wherein the furan ring is unsubstituted or substituted with 1 or 2 alkyl groups wherein each alkyl group is independently selected,  $R^7$  is selected from the group consisting of:  $-CF_3$ , alkyl and cycloalkyl, and  $R^8$  is H.

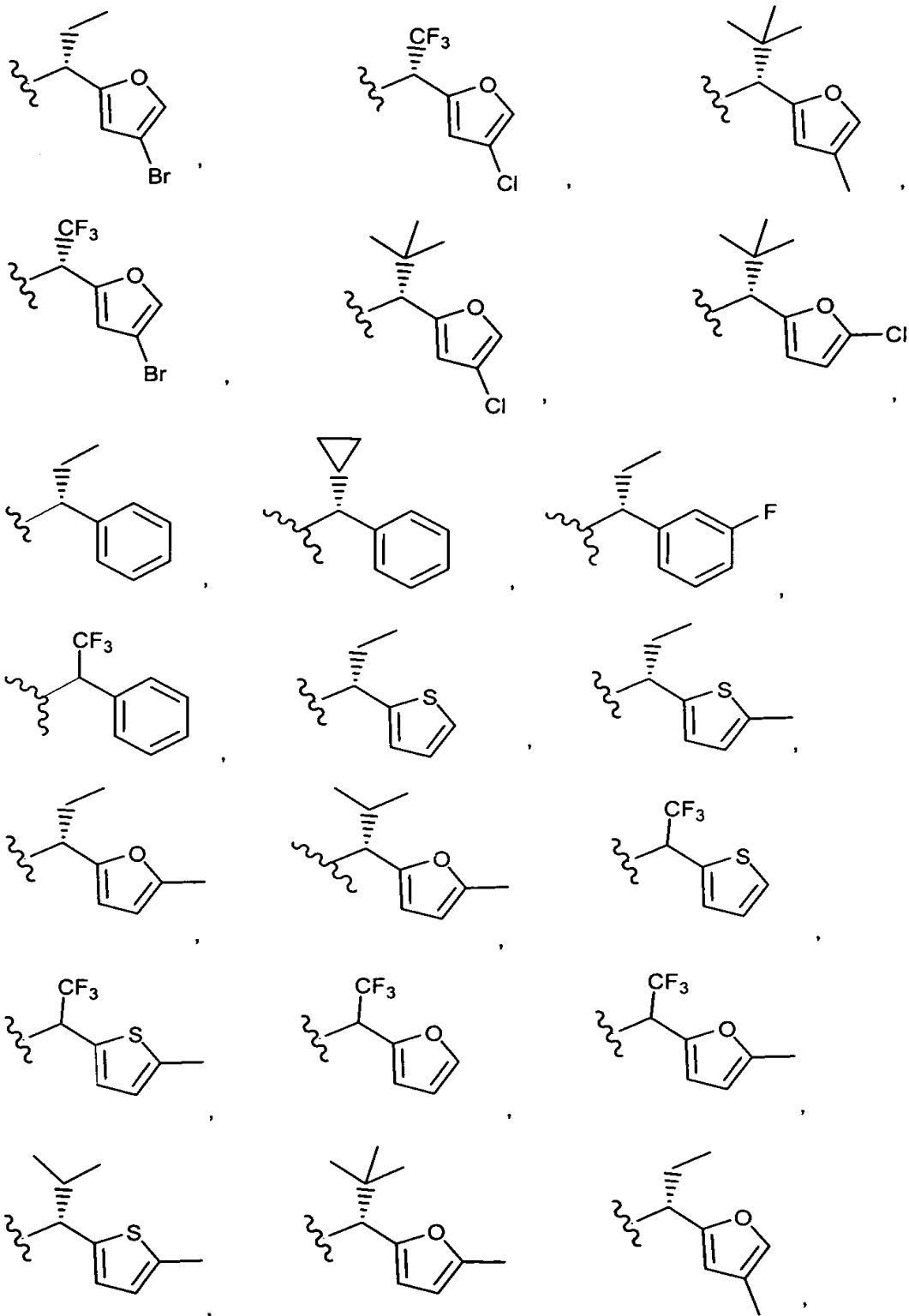
4. The compound of Claim 1 wherein substituent A is:

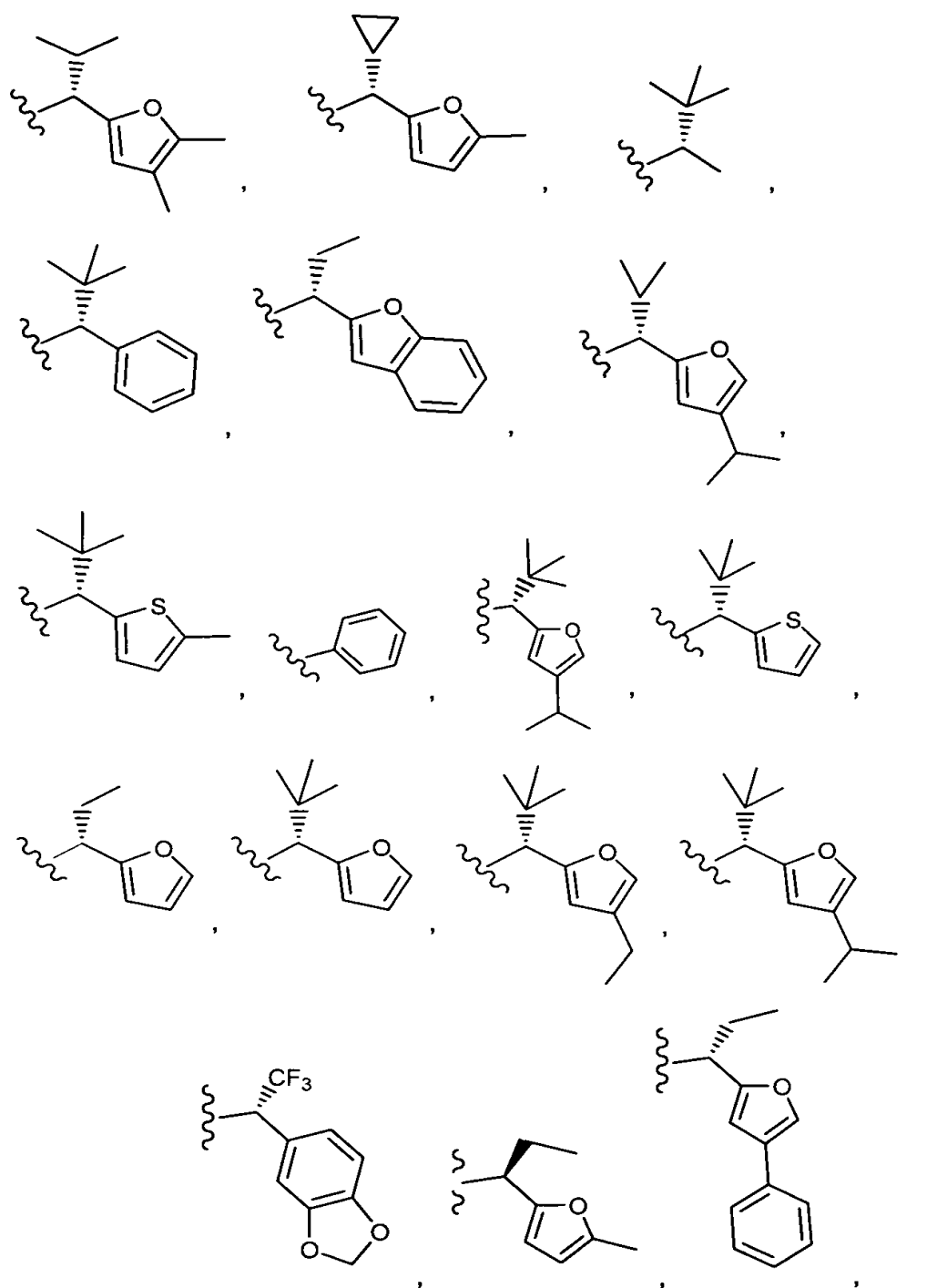


wherein the furan ring is substituted with 1 or 2 alkyl groups independently selected from the group consisting of methyl, ethyl and isopropyl,  $R^7$  is selected from the group consisting of: ethyl, isopropyl and t-butyl, and  $R^8$  is H.

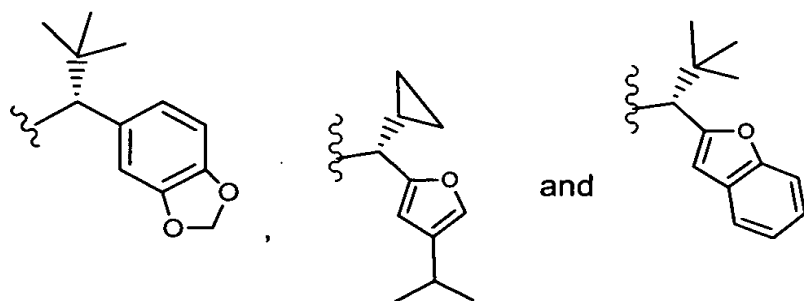
5. The compound of Claim 1 wherein A is selected from the group consisting of:



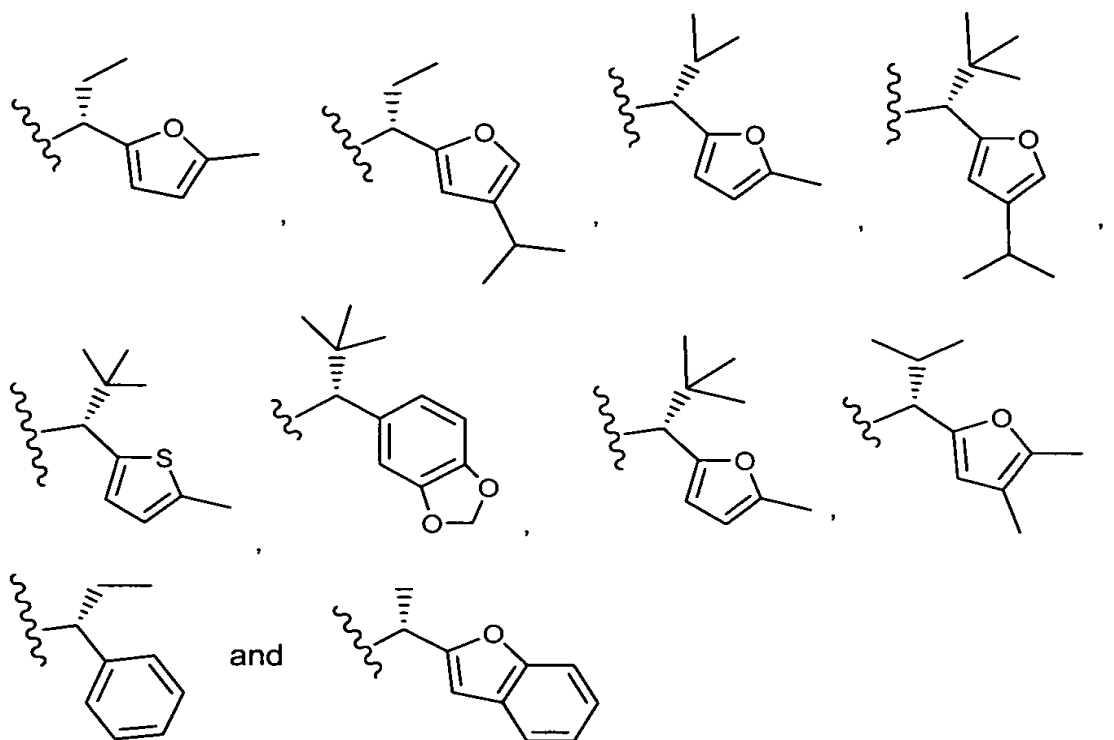




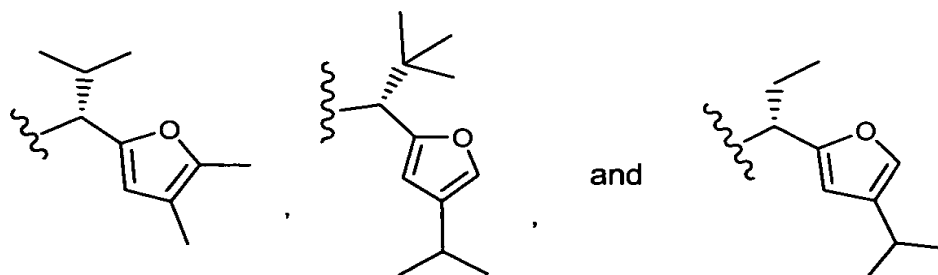




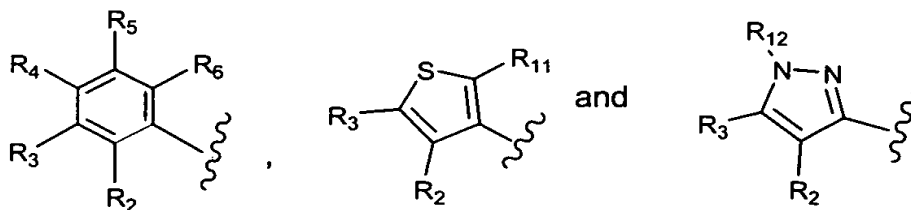
6. The compound of claim 1 wherein A is selected from the group consisting of:



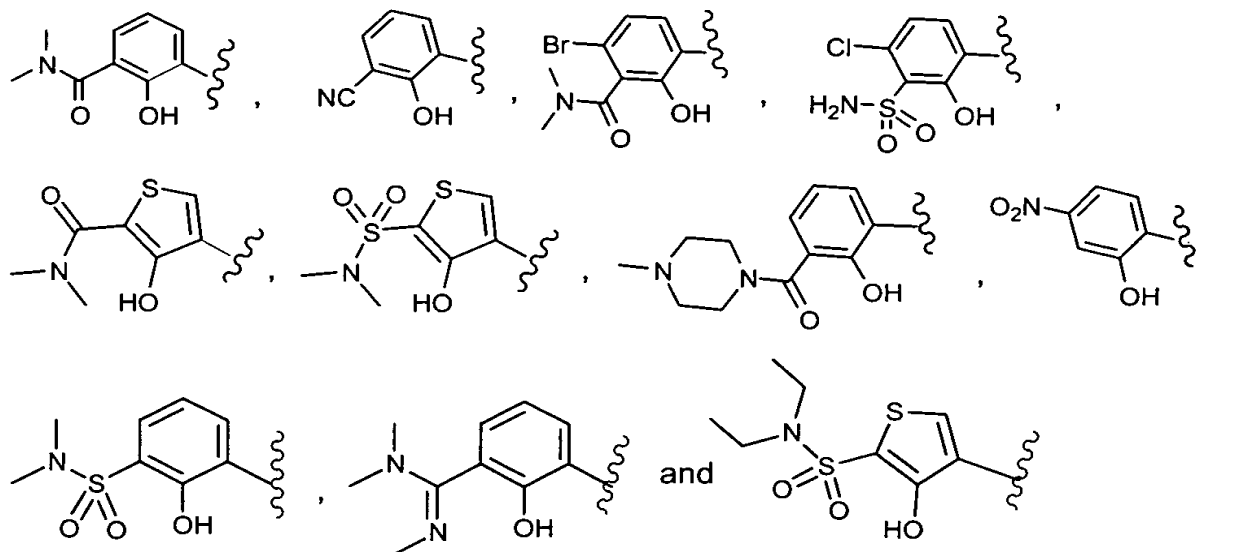
7. The compound of Claim 1 wherein substituent A is selected from the group consisting of:



8. The compound of Claim 1 wherein B is selected from the group consisting of:

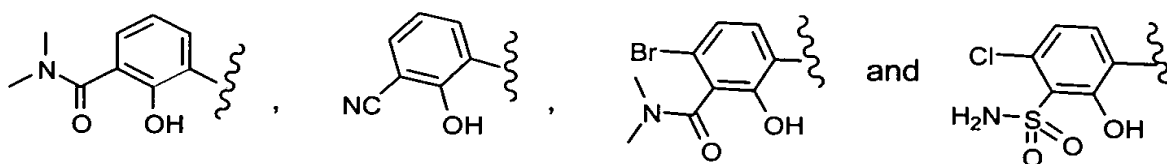


5 9. The compound of Claim 1 wherein B is selected from the group consisting of:



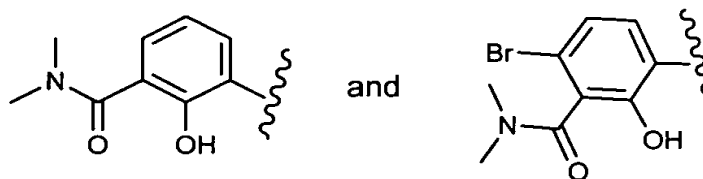
10

10. The compound of Claim 1 wherein B is selected from the group consisting of:

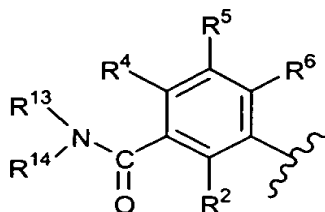


15

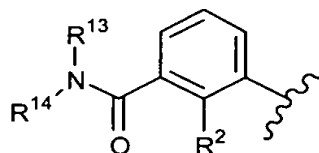
11. The compound of Claim 1 wherein B is selected from the group consisting of:



5 12. The compound of Claim 1 wherein B is

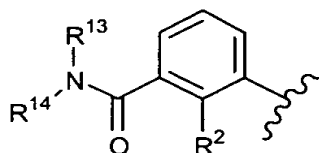


13. The compound of Claim 1 wherein B is:



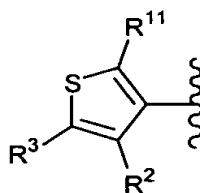
10 wherein R<sup>2</sup> is -OH.

14. The compound of Claim 1 wherein B is:



15 wherein R<sup>2</sup> is -OH, and R<sup>13</sup> and R<sup>14</sup> are independently selected from the group consisting of H and alkyl.

15. The compound of Claim 1 wherein B is



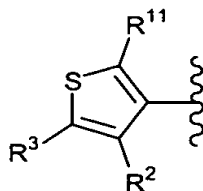
16. The compound of Claim 15 wherein  $R^{11}$  is H.

17. The compound of Claim 16 wherein  $R^2$  is  $-OH$ .

5 18. The compound of Claim 17 wherein  $R^3$  is  $-C(O)NR^{13}R^{14}$ .

19. The compound of Claim 17 wherein  $R^3$  is  $-S(O)_tNR^{13}R^{14}$ .

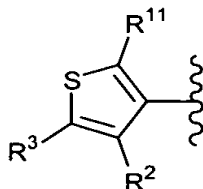
20. The compound of Claim 1 wherein B is:



10

wherein  $R^2$  is  $-OH$ ,  $R^3$  is  $-C(O)NR^{13}R^{14}$ ,  $R^{11}$  is H or methyl, and  $R^{13}$  and  $R^{14}$  are independently selected from the group consisting of: H, alkyl, unsubstituted cycloalkyl, substituted cycloalkyl, unsubstituted heteroaryl and substituted heteroaryl.

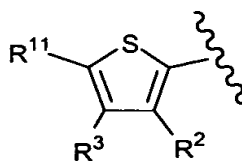
15 21. The compound of Claim 1 wherein B is:



wherein  $R^2$  is  $-OH$ ,  $R^3$  is  $-S(O)_tNR^{13}R^{14}$ ,  $R^{11}$  is H or methyl, and  $R^{13}$  and  $R^{14}$  are independently selected from the group consisting of H, alkyl, unsubstituted cycloalkyl and substituted cycloalkyl.

20

22. The compound of Claim 1 wherein B is:



23. The compound of Claim 22 in  $R^{11}$  is H.

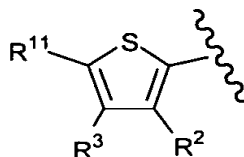
25

24. The compound of Claim 23 wherein  $R^2$  is  $-OH$ .

25. The compound of Claim 24 wherein  $R^3$  is  $-C(O)NR^{13}R^{14}$ .

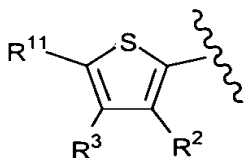
5 26. The compound of Claim 24 wherein  $R^3$  is  $-S(O)_tNR^{13}R^{14}$ .

27. The compound of Claim 1 wherein B is:



10 wherein  $R^2$  is  $-OH$ ,  $R^3$  is  $-C(O)NR^{13}R^{14}$ ,  $R^{11}$  is H, and  $R^{13}$  and  $R^{14}$  are independently selected from the group consisting of: H, alkyl, unsubstituted heteroaryl and substituted heteroaryl.

28. The compound of Claim 1 wherein B is:



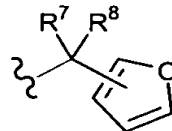
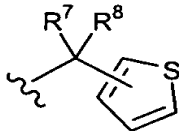
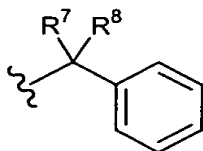
15 wherein  $R^2$  is  $-OH$ ,  $R^3$  is  $-S(O)_tNR^{13}R^{14}$ ,  $R^{11}$  is H, and  $R^{13}$  and  $R^{14}$  are independently selected from the group consisting of H and alkyl.

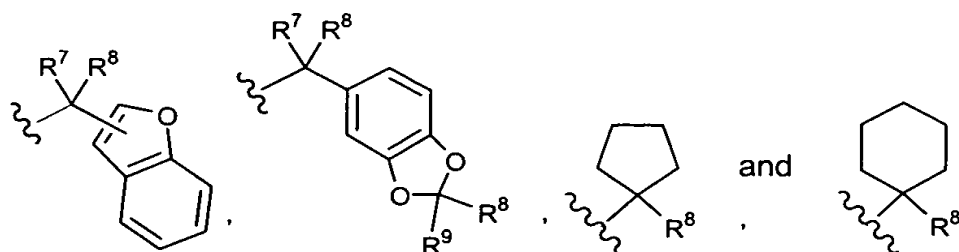
29. The compound of Claim 1 wherein:

(1) substituent A in formula IA is selected from the group consisting

20 of:

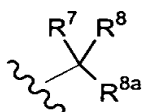
(a)





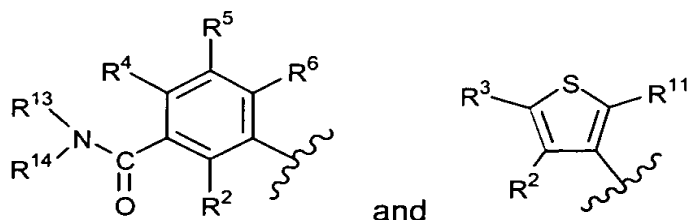
wherein the above rings are unsubstituted, or the above rings are substituted with 1 to 3 substituents independently selected from the group consisting of: F, Cl, Br, alkyl, cycloalkyl, and  $-\text{CF}_3$ ;  $\text{R}^7$  is selected from the group consisting of: H,  $-\text{CF}_3$ ,  $-\text{CF}_2\text{CH}_3$ , methyl, ethyl, isopropyl, cyclopropyl and t-butyl; and  $\text{R}^8$  is H; and

(b)



wherein  $\text{R}^7$  is selected from the group consisting of: H,  $-\text{CF}_3$ ,  $-\text{CF}_2\text{CH}_3$ , methyl, ethyl, isopropyl, cyclopropyl and t-butyl; and  $\text{R}^8$  is H; and  $\text{R}^{8a}$  is as defined in Claim 1;

(2) substituent B in formula IA is selected from the group consisting of:



wherein:

$\text{R}^2$  is selected from the group consisting of: H, OH,  $-\text{NHC}(\text{O})\text{R}^{13}$  and  $-\text{NHSO}_2\text{R}^{13}$ ;

$\text{R}^3$  is selected from the group consisting of:  $-\text{C}(\text{O})\text{NR}^{13}\text{R}^{14}$ ,  $-\text{SO}_2\text{NR}^{13}\text{R}^{14}$ ,  $-\text{NO}_2$ , cyano, and  $-\text{SO}_2\text{R}^{13}$ ;

$\text{R}^4$  is selected from the group consisting of: H,  $-\text{NO}_2$ , cyano, alkyl, halogen and  $-\text{CF}_3$ ;

$\text{R}^5$  is selected from the group consisting of: H,  $-\text{CF}_3$ ,  $-\text{NO}_2$ , halogen and cyano;

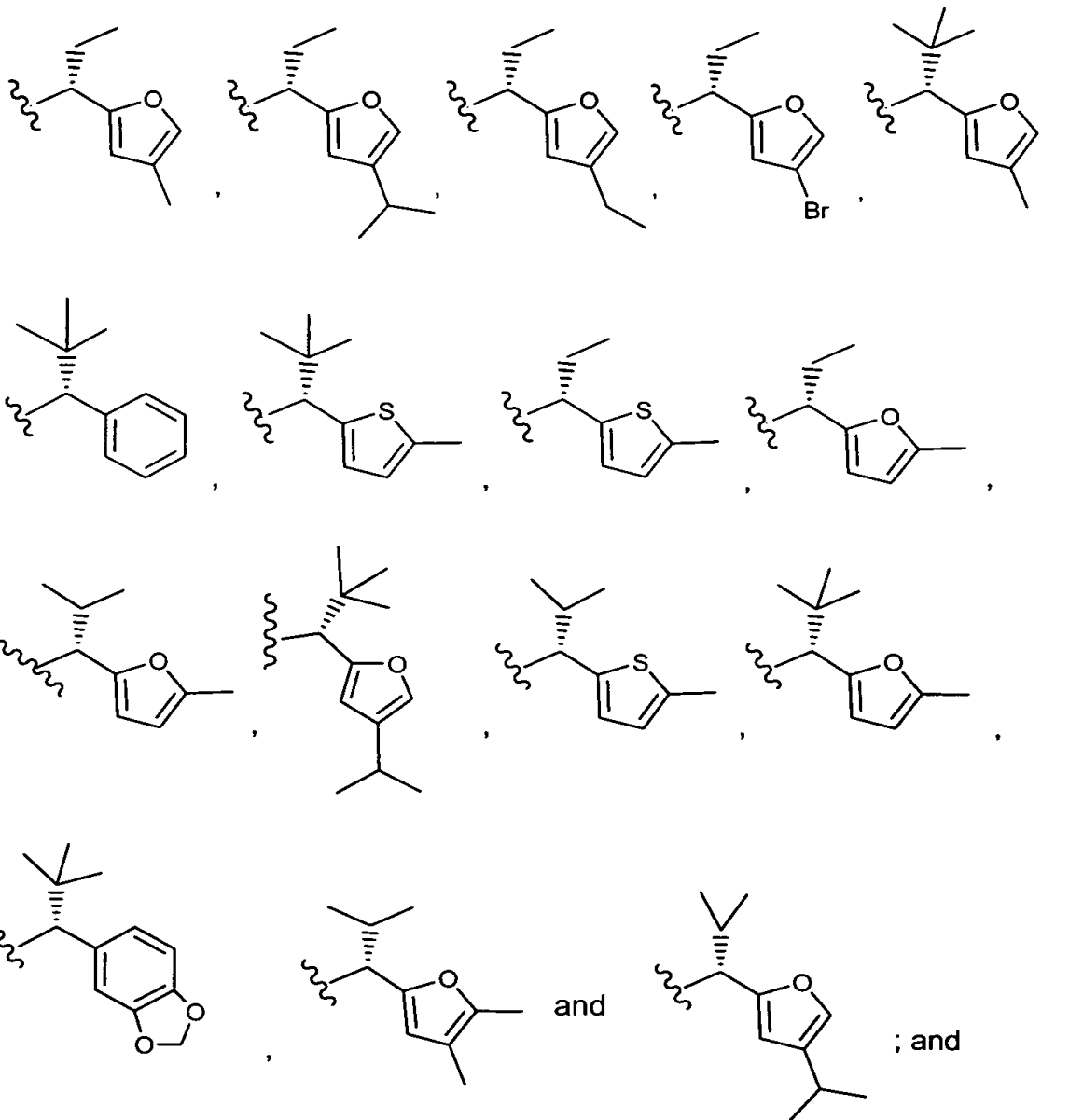
$\text{R}^6$  is selected from the group consisting of: H, alkyl and  $-\text{CF}_3$ ;

$\text{R}^{11}$  is selected from the group consisting of: H, halogen and alkyl; and

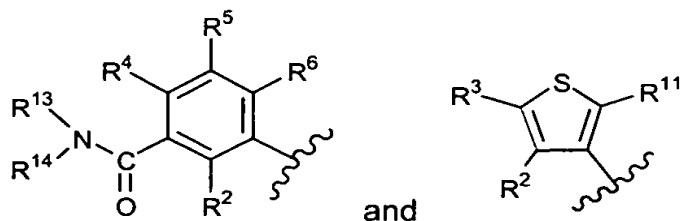
each  $R^{13}$  and  $R^{14}$  is independently selected from the group consisting of: H, unsubstituted alkyl.

30. The compound of Claim 1 wherein:

- 5 (1) substituent A in formula IA is selected from the group consisting of:



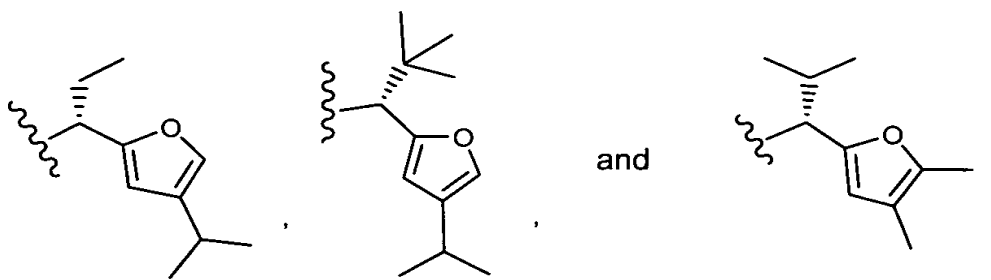
(2) substituent B in formula IA is selected from the group consisting of:



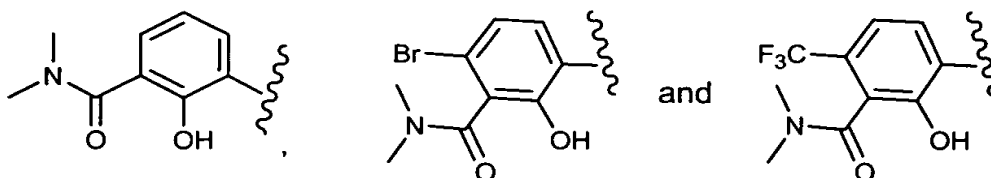
wherein:

- 5  $R^2$  is  $-OH$ ;  
 $R^3$  is selected from the group consisting of:  $-SO_2NR^{13}R^{14}$  and  $-CONR^{13}R^{14}$ ;  
 $R^4$  is selected from the group consisting of: H, Br,  $-CH_3$ , ethyl and  $-CF_3$ ;  
 $R^5$  is selected from the group consisting of: H and cyano;  
 $R^6$  is selected from the group consisting of: H,  $-CH_3$  and  $-CF_3$ ;  
10  $R^{11}$  is H; and  
 $R^{13}$  and  $R^{14}$  are independently selected from the group consisting of H and methyl.

31. The compound of Claim 1 wherein substituent A is selected from the group consisting of:

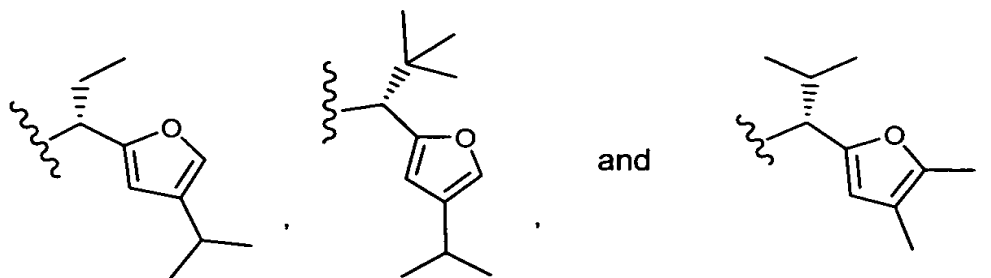


and substituent B is selected from the group consisting of:





32. The compound of Claim 1 wherein substituent A is selected from the group consisting of:



and substituent B is selected from the group consisting of:



5

33. The compound of Claim 1 wherein g is 1.

34. The compound of Claim 1 wherein g is 2.

10

35. The compound of Claim 31 wherein g is 1.

36. The compound of Claim 32 wherein g is 2.

15

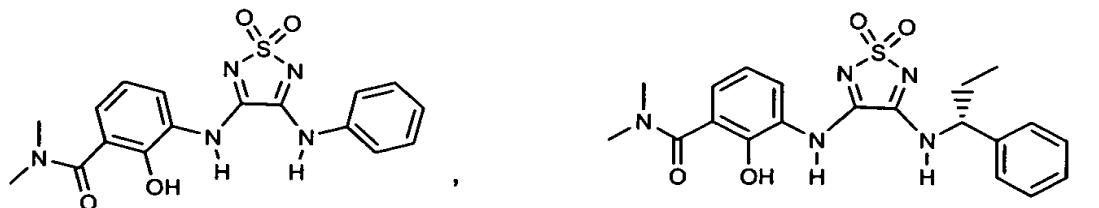
37. A pharmaceutically acceptable salt of a compound of Claim 1.

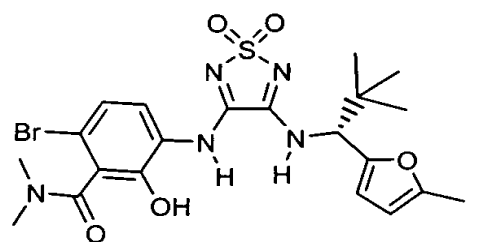
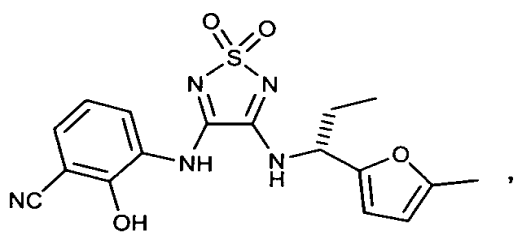
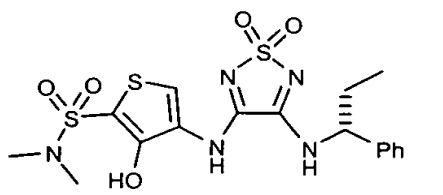
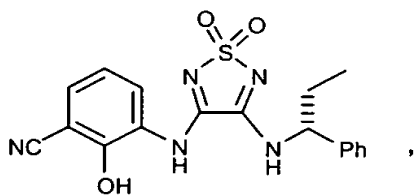
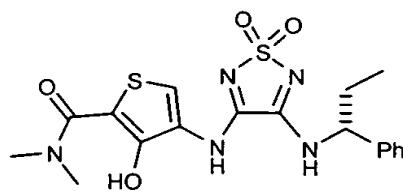
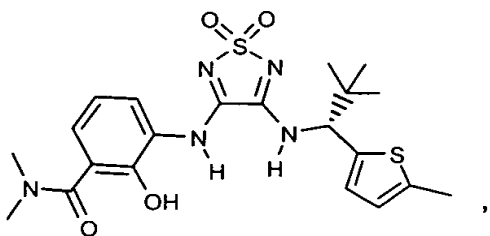
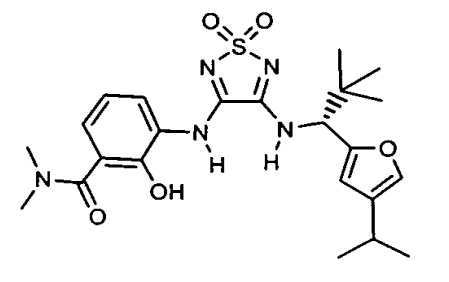
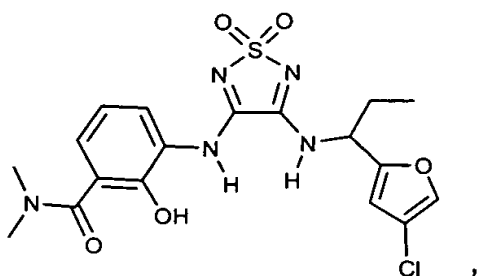
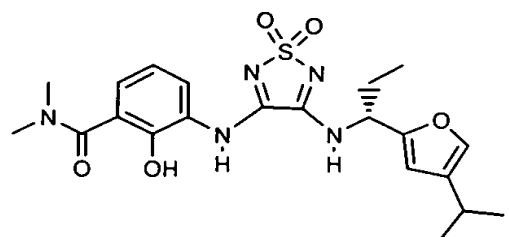
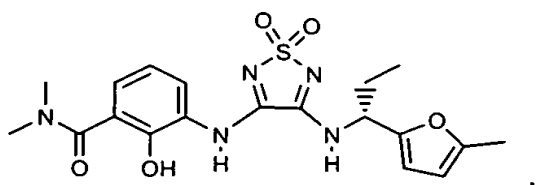
38. A sodium salt of a compound of Claim 1.

39. A calcium salt of a compound of Claim 1.

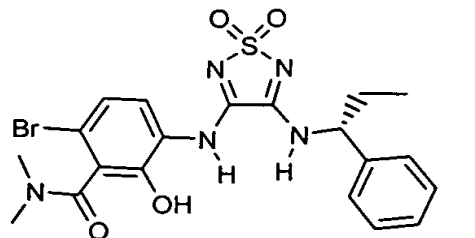
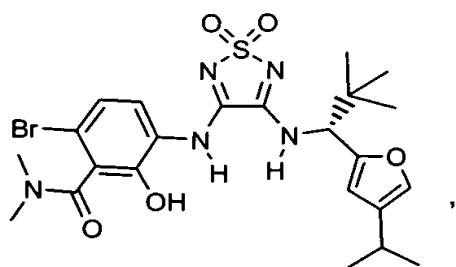
20

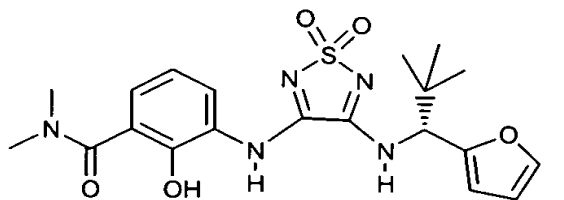
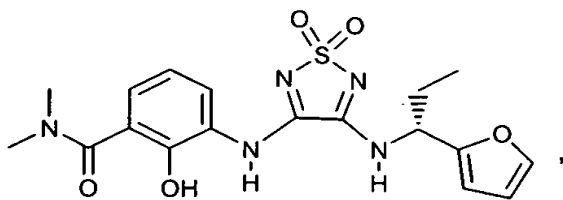
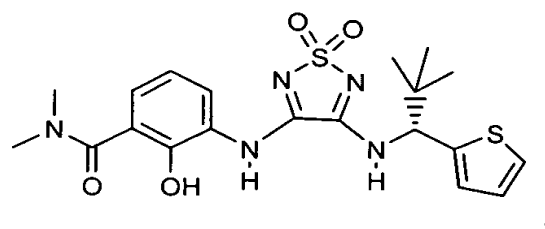
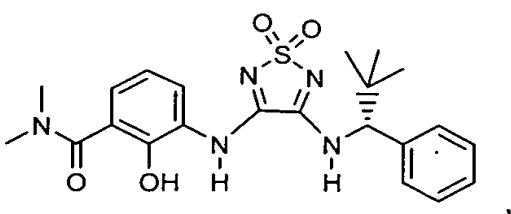
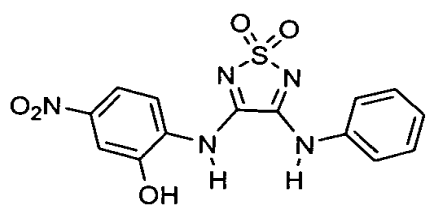
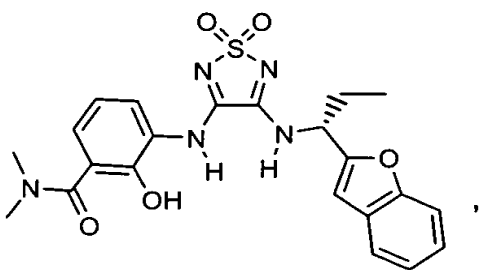
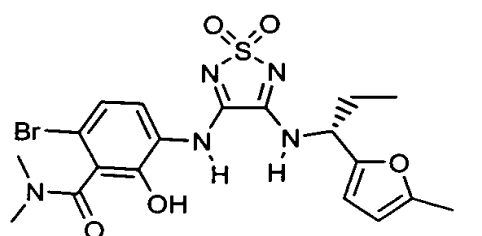
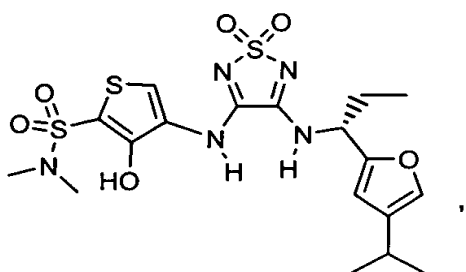
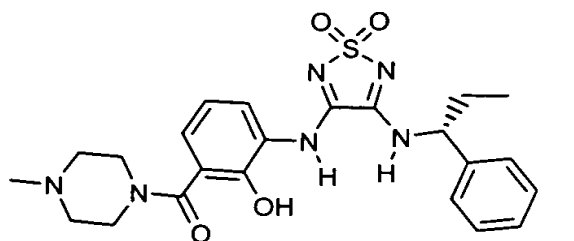
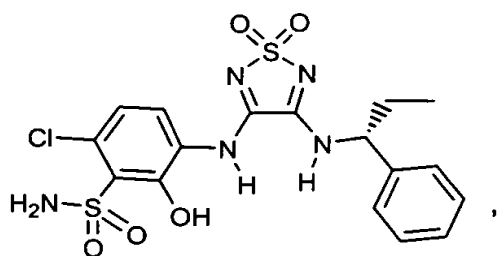
40. The compound of Claim 1 selected from the group consisting of:



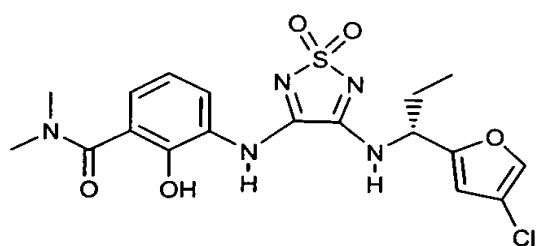
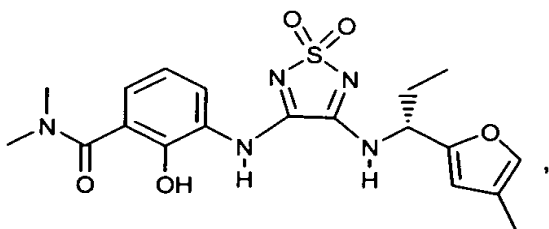


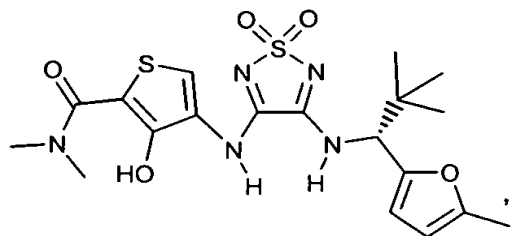
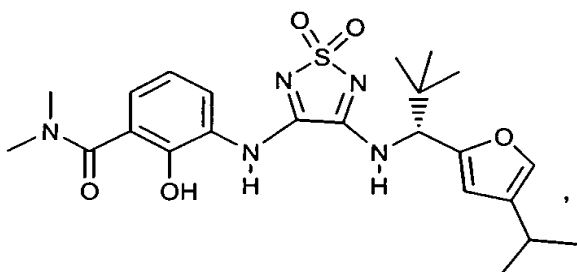
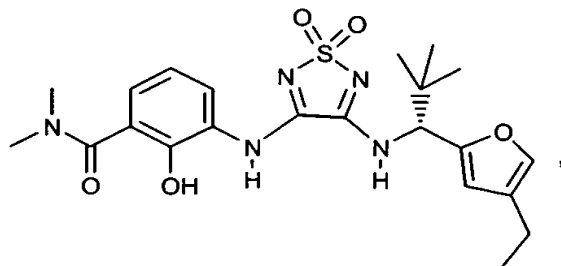
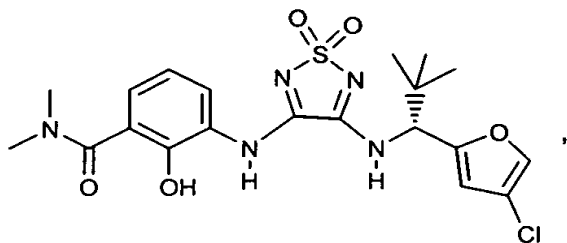
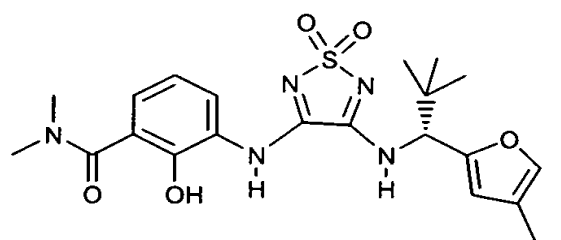
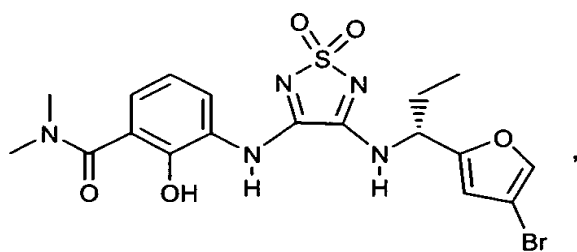
5



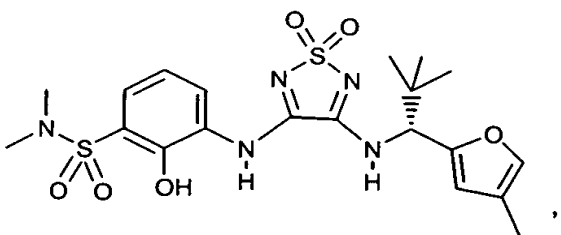
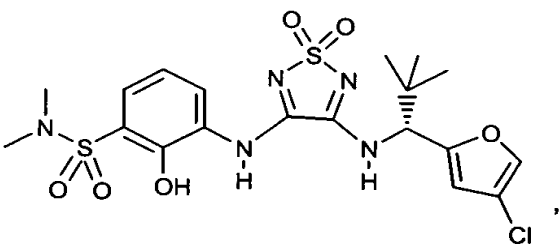
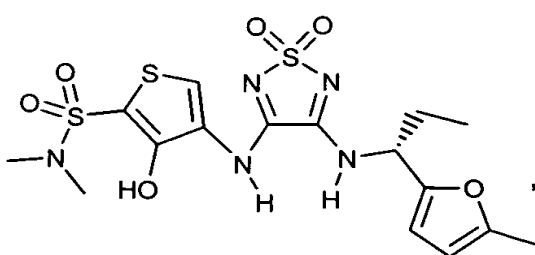
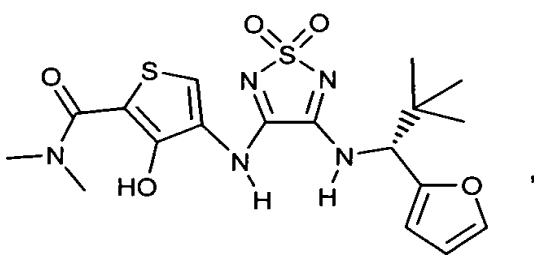


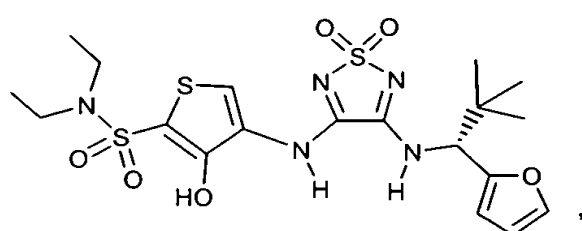
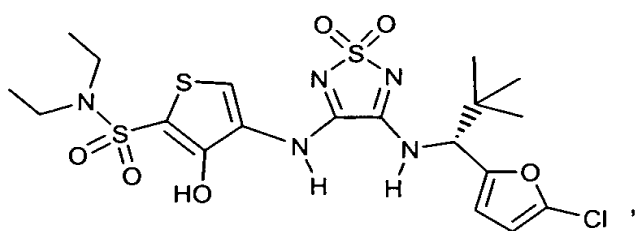
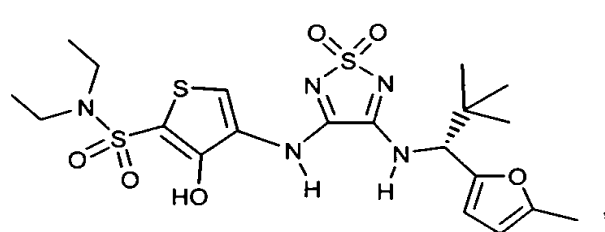
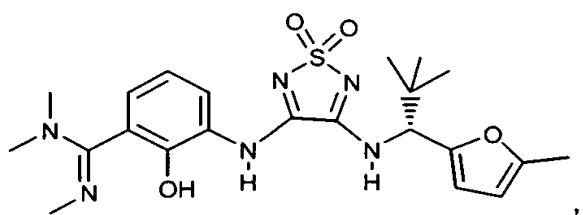
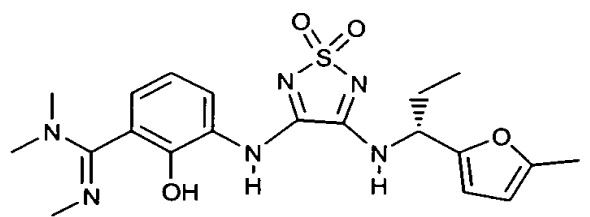
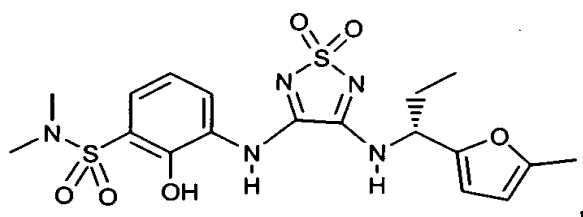
5



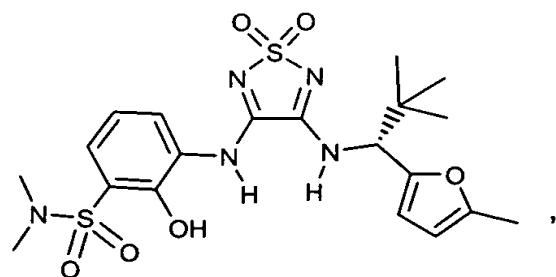
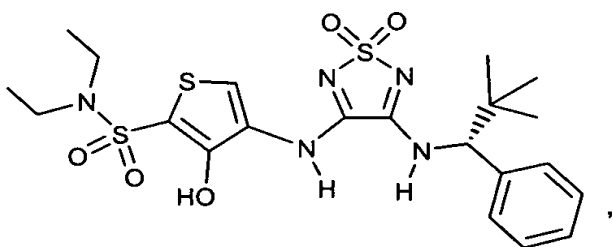
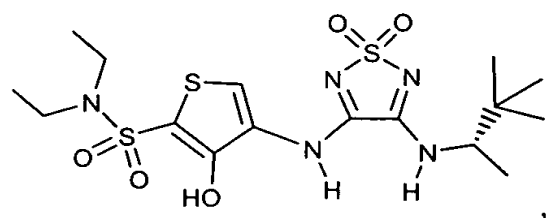
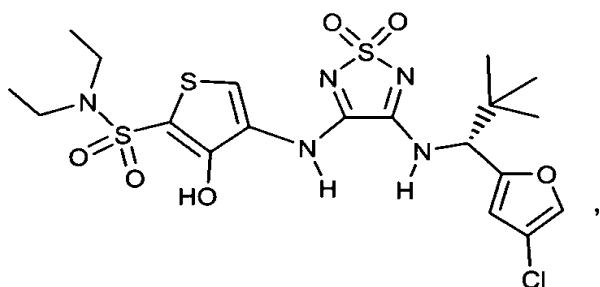


5

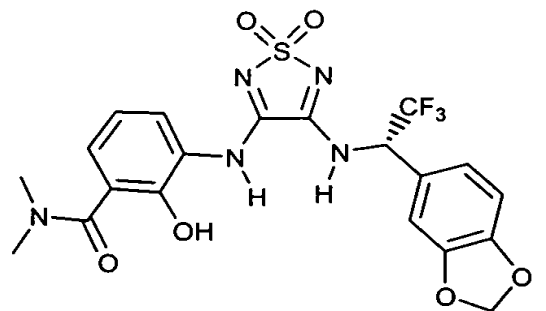
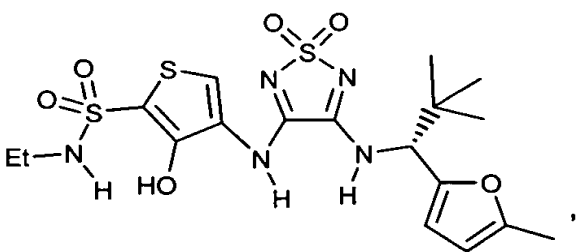
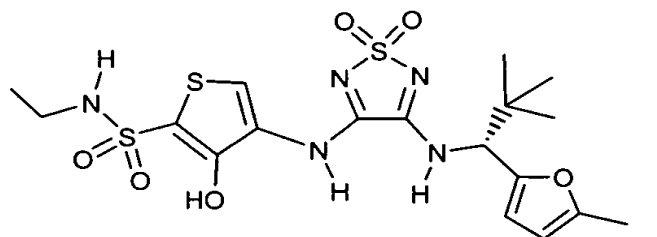
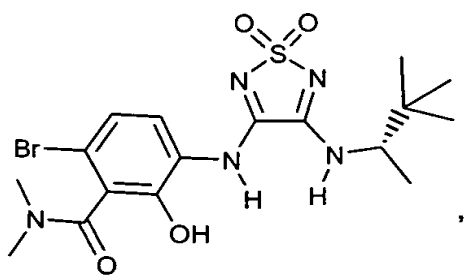
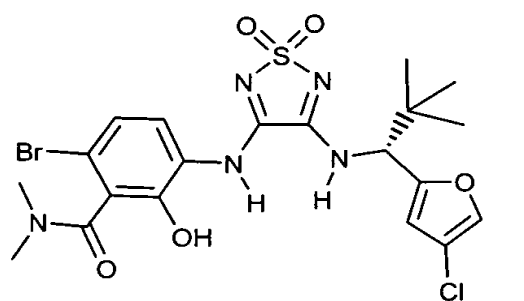
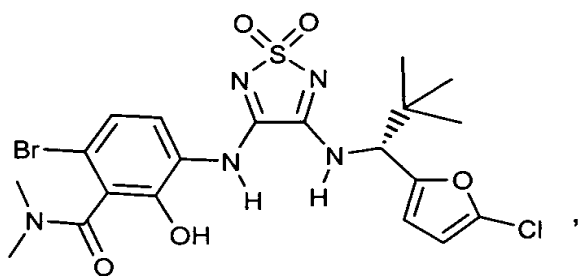
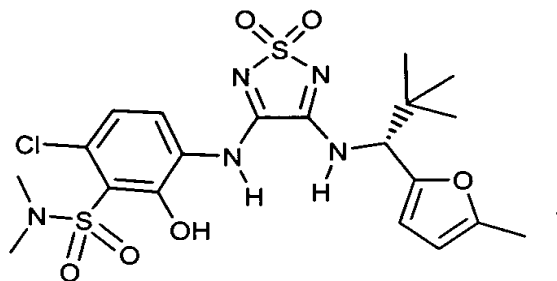
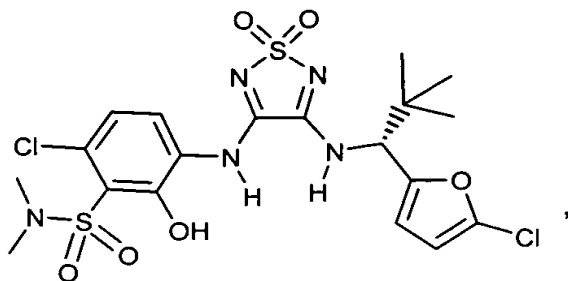
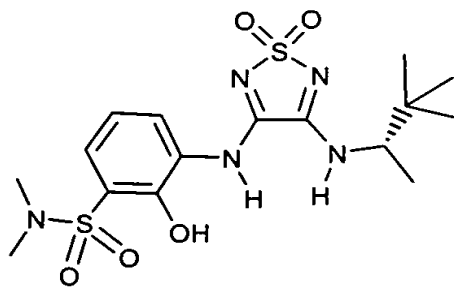
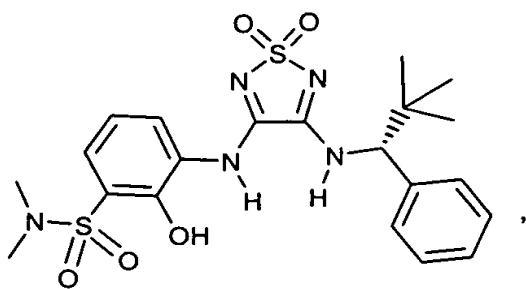


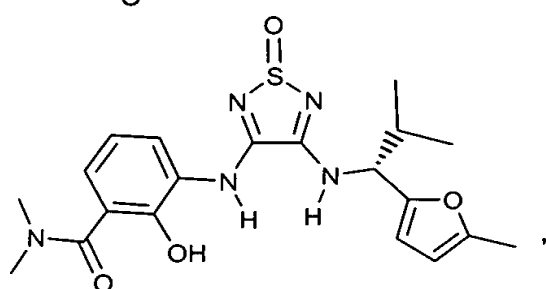
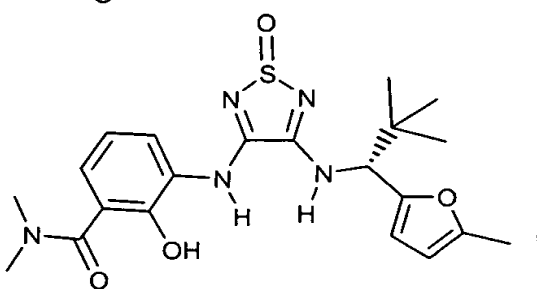
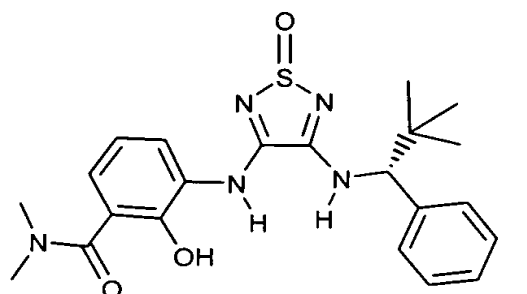
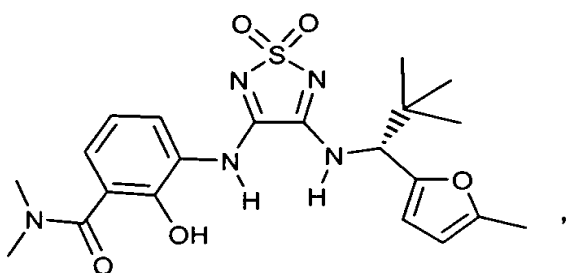
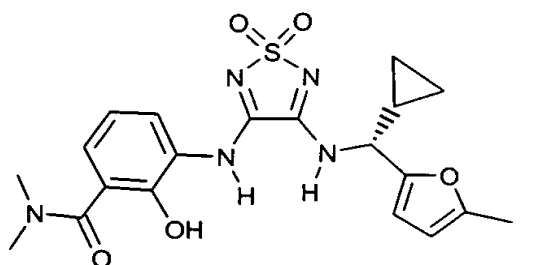
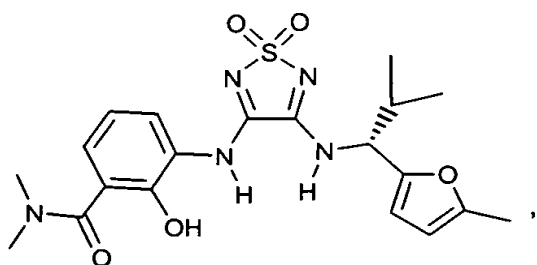


5

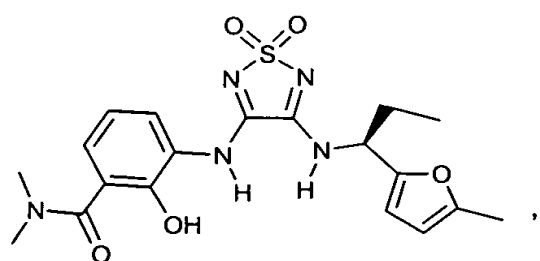
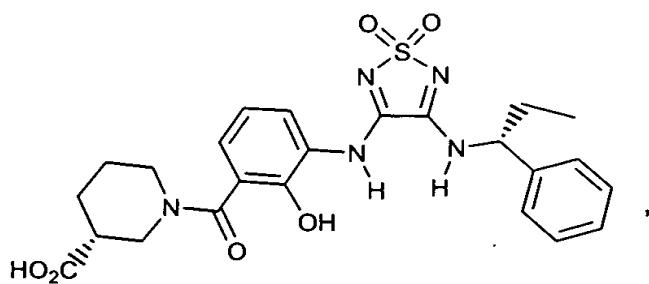
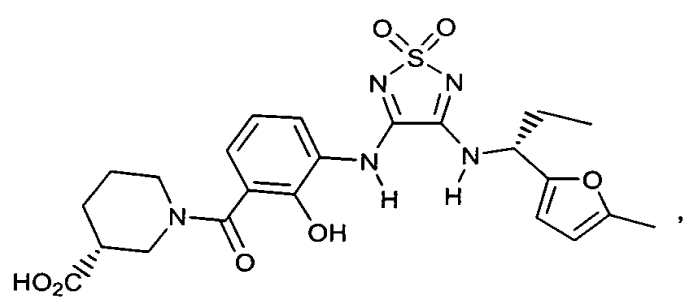
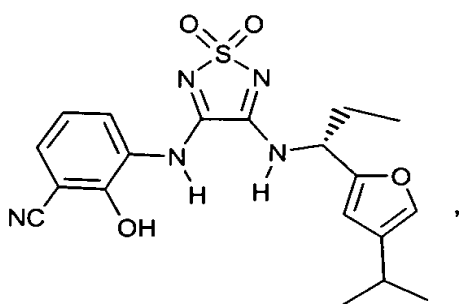


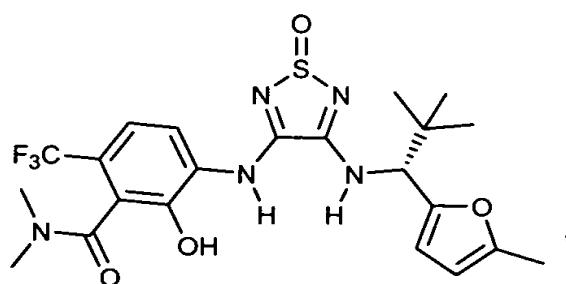
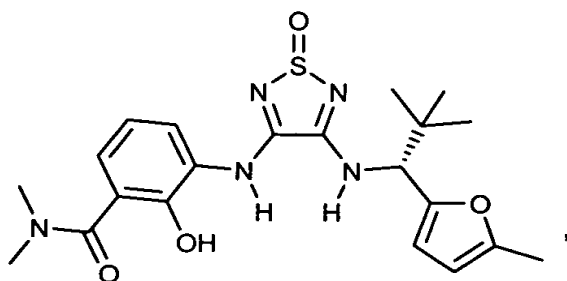
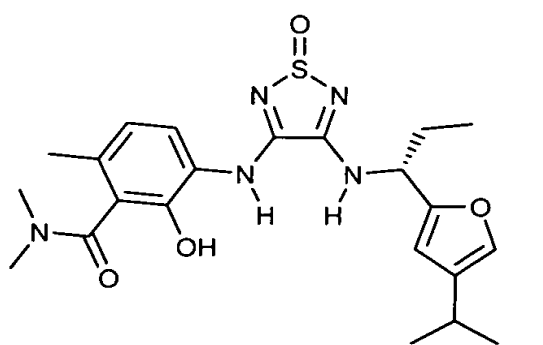
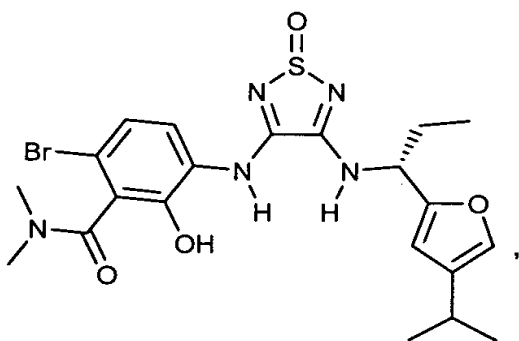
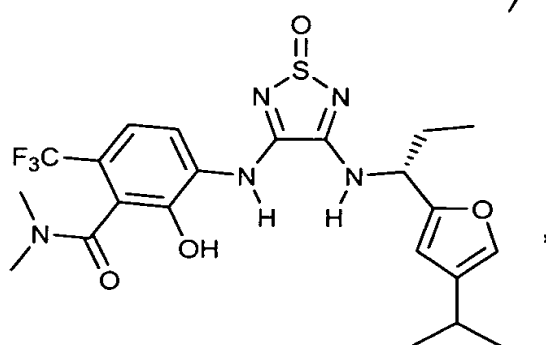
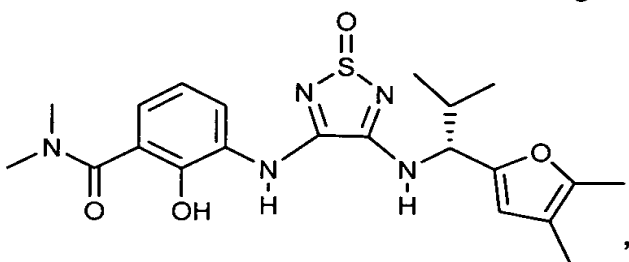
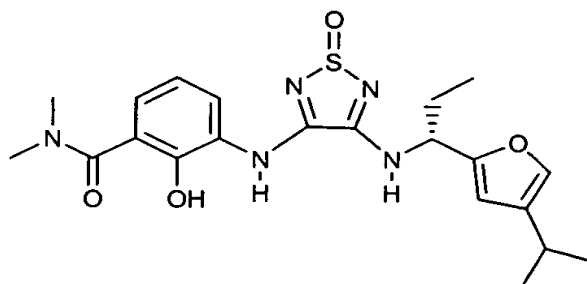
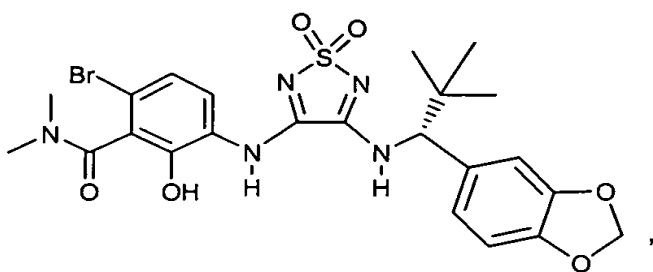
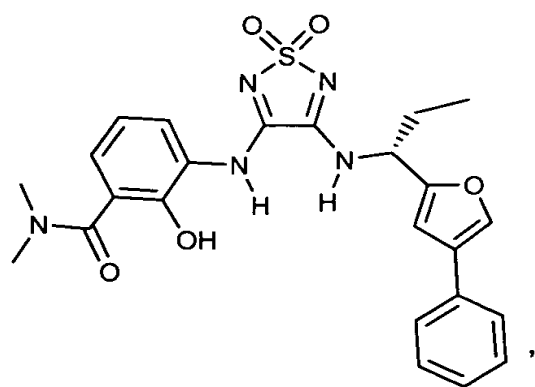
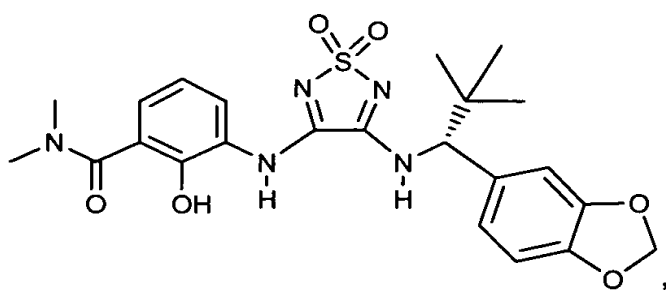
10



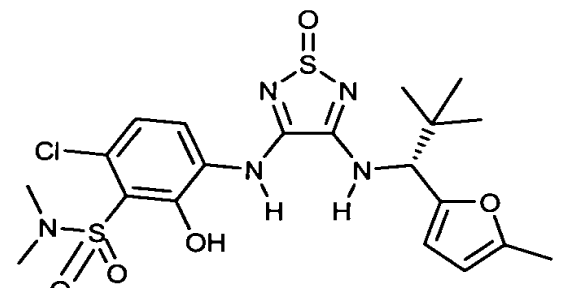
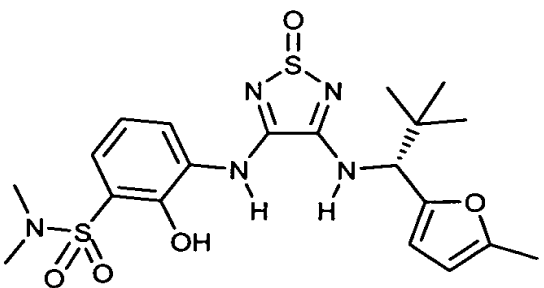
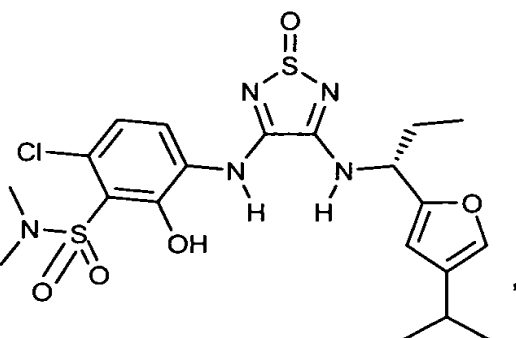
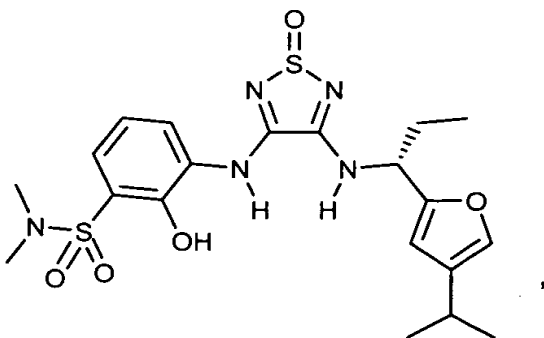
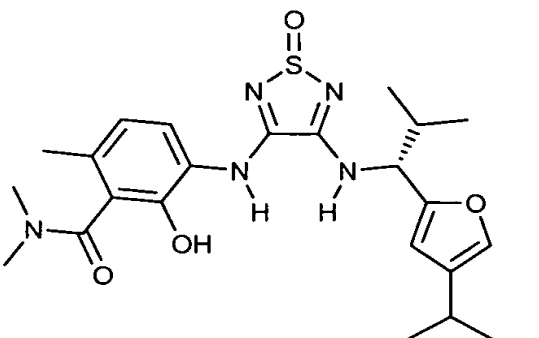
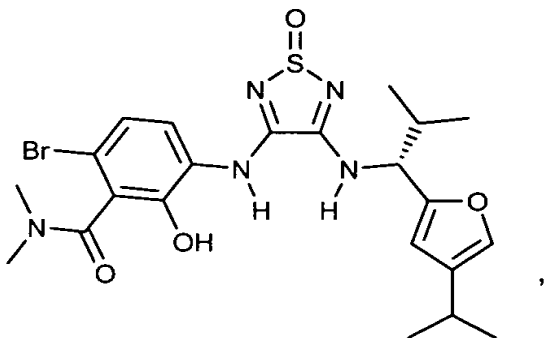
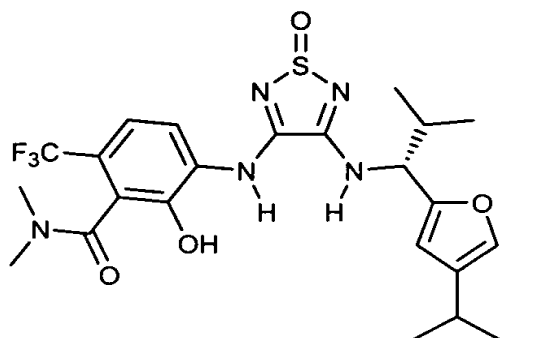
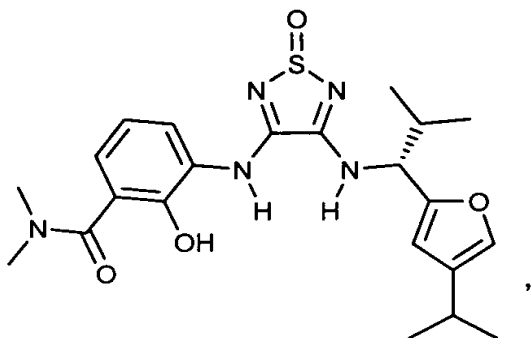
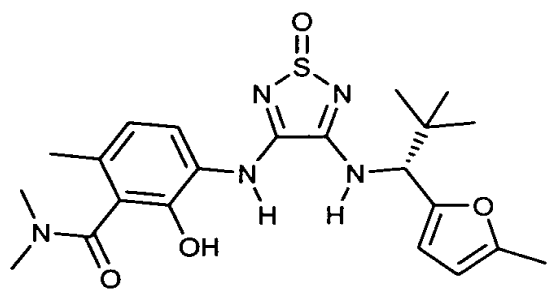
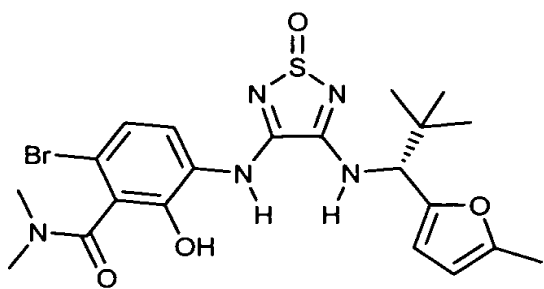


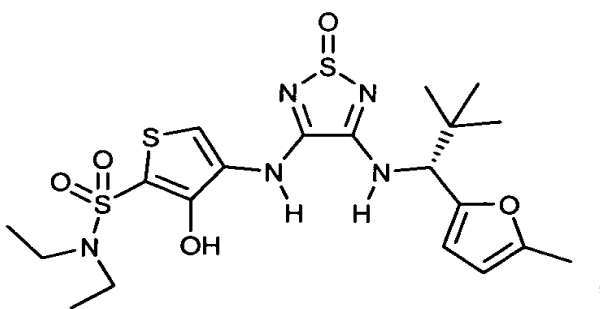
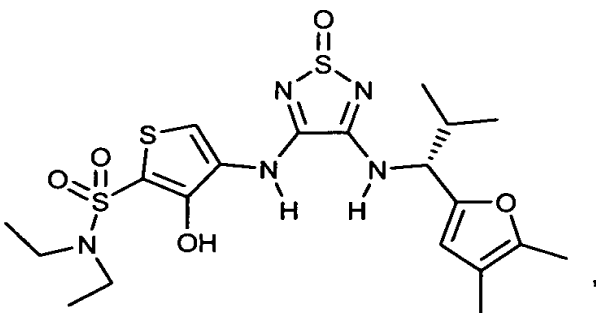
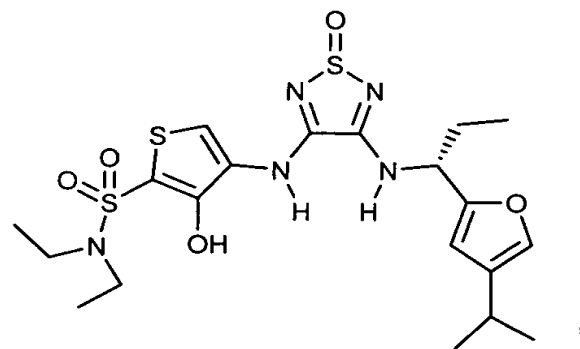
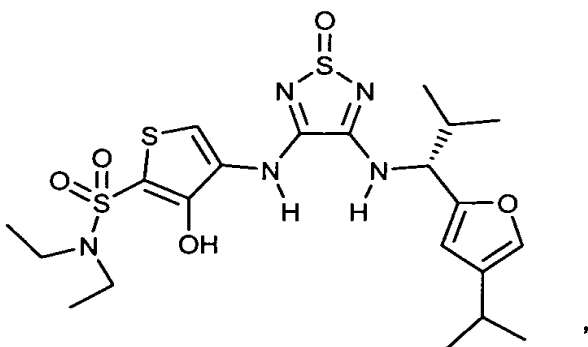
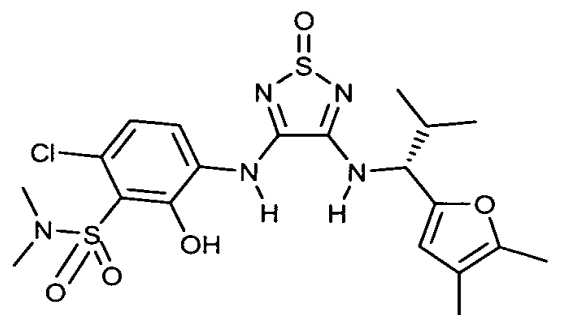
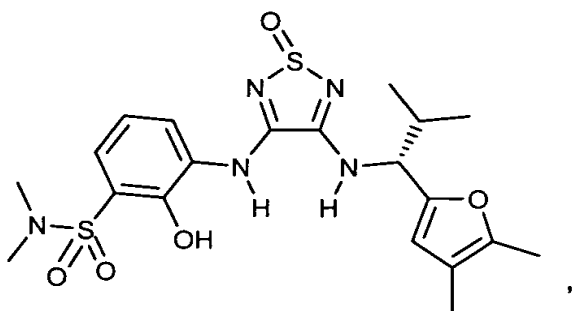
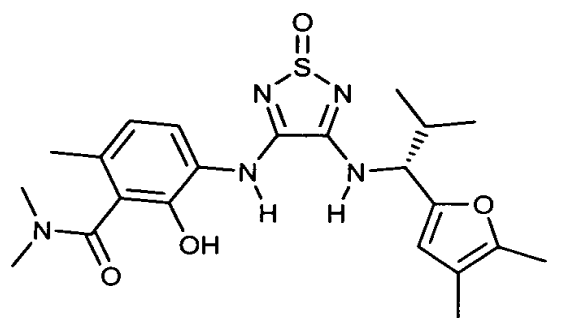
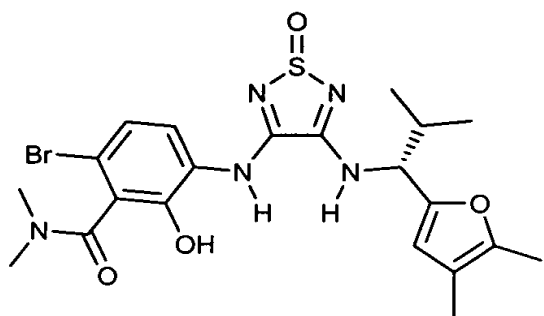
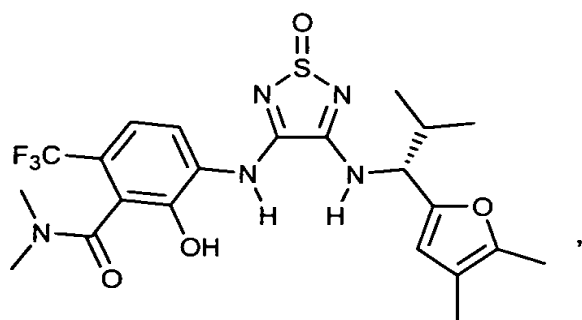
5





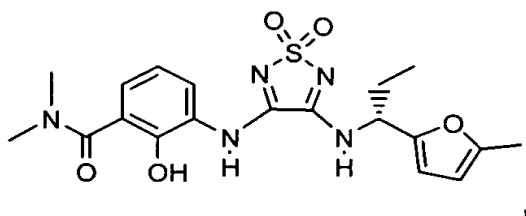




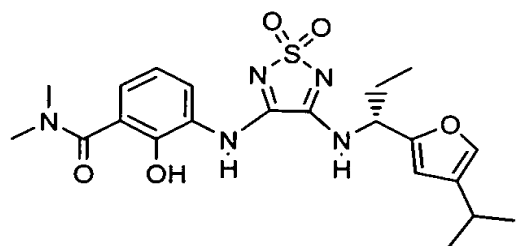


5

41. The compound of Claim 1 selected from the group consisting of:

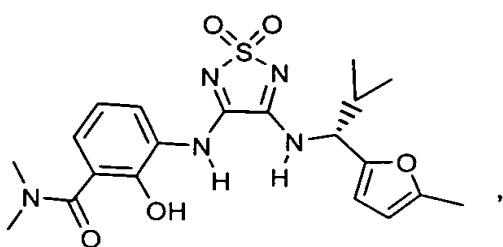


(a1)

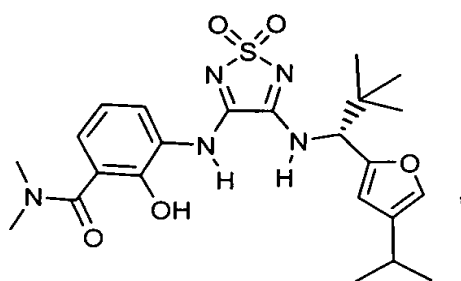


(a2)

5

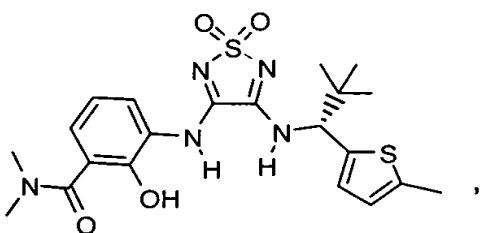


(a3)

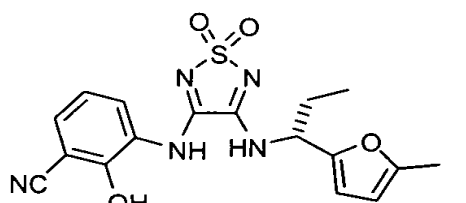


(a4)

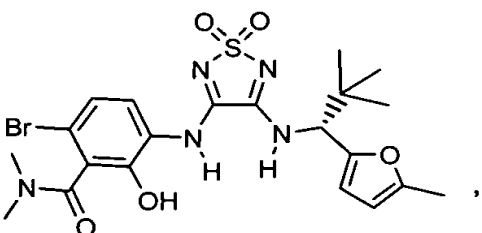
10



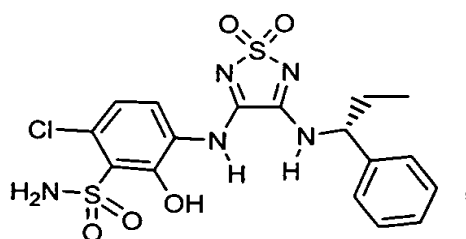
(a5)



(a6)

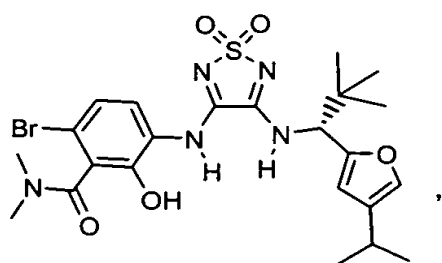


(a7)

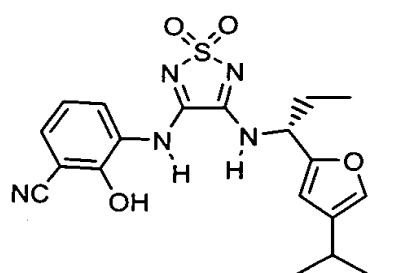


(a8)

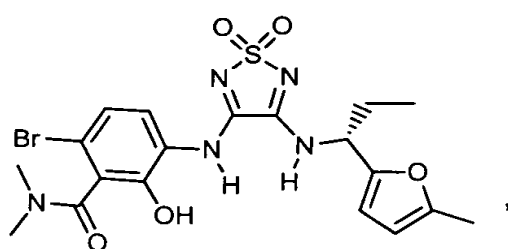
15



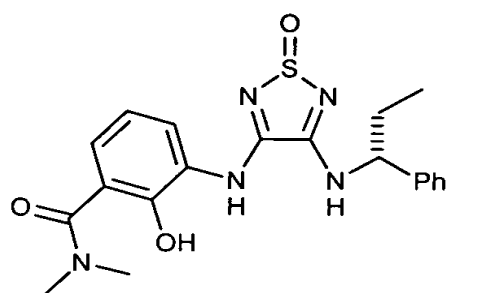
(a9)



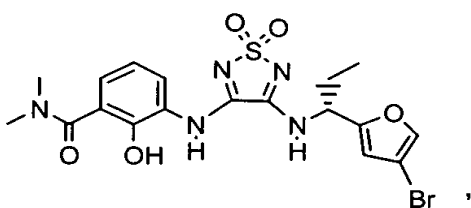
(a10)



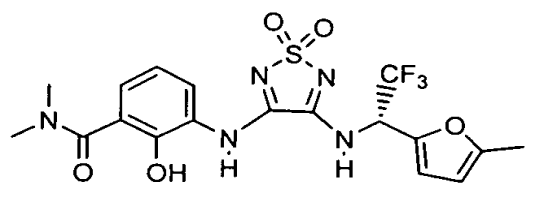
(a11)



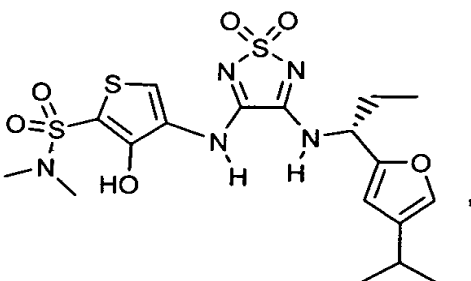
(a12)



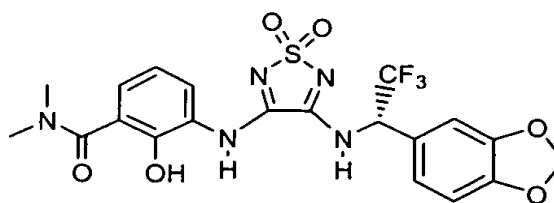
(a13)



(a14)



(a15)

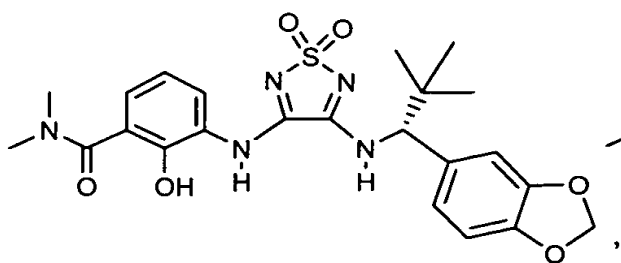


(a16)

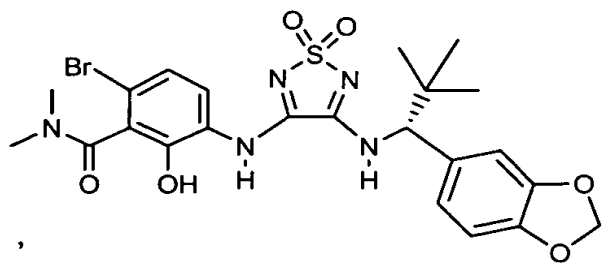
5

10

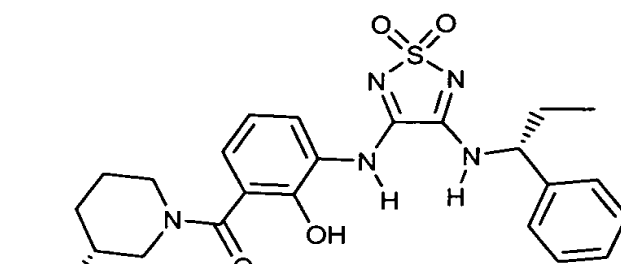
15



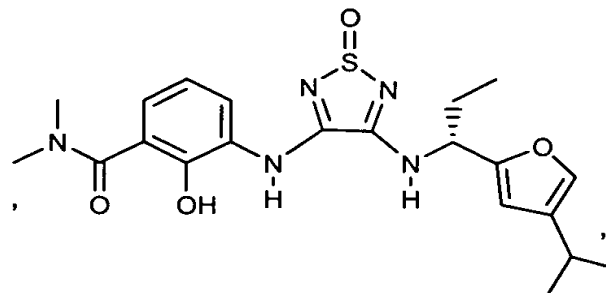
(a17)



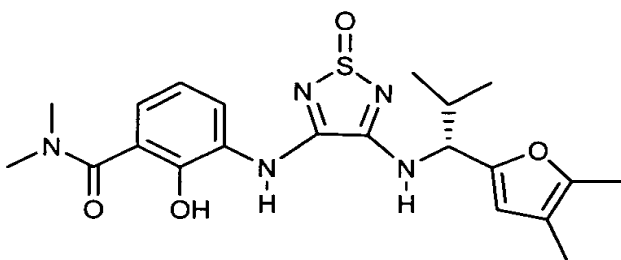
(a18)



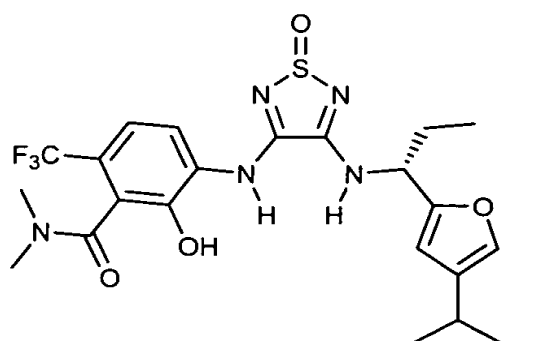
(a19)



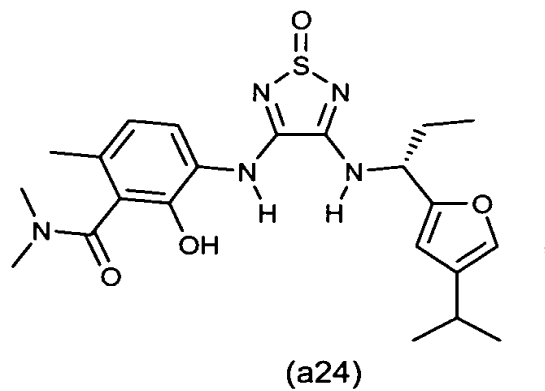
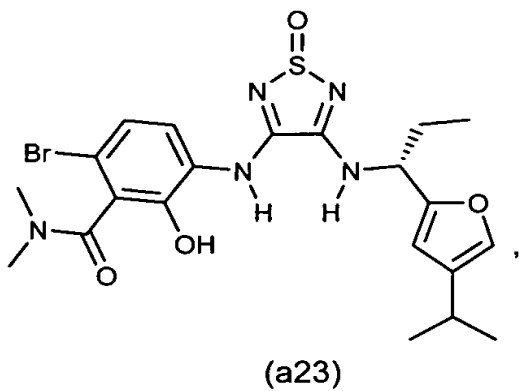
(a20)



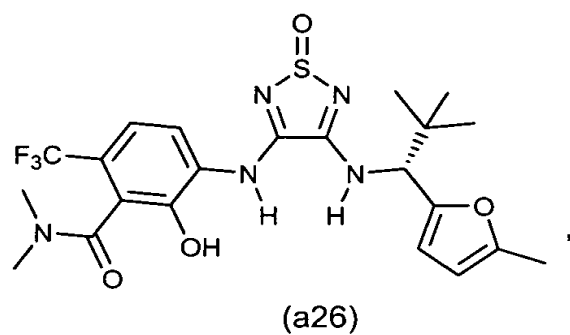
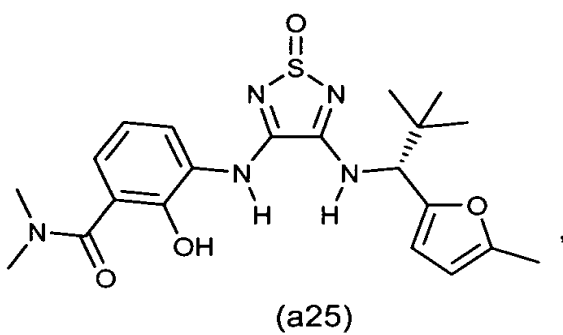
(a21)



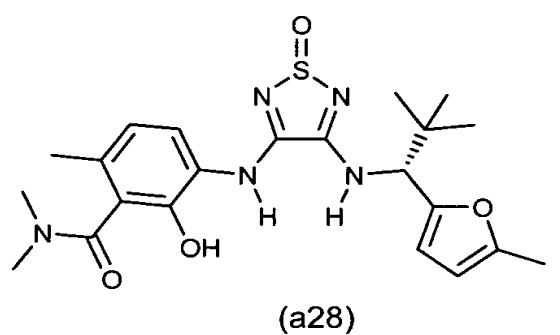
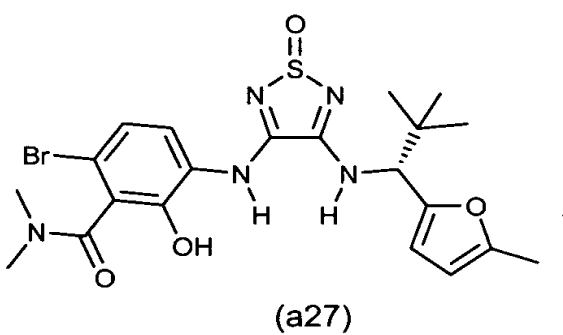
(a22)

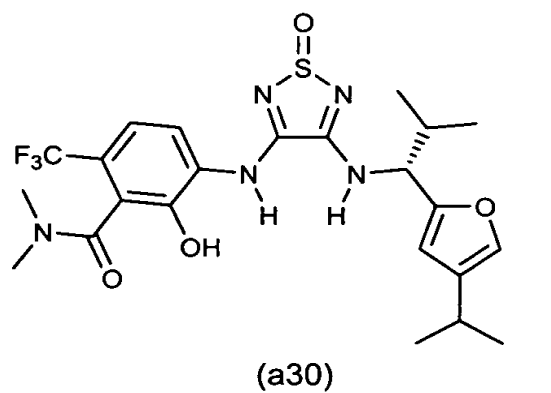
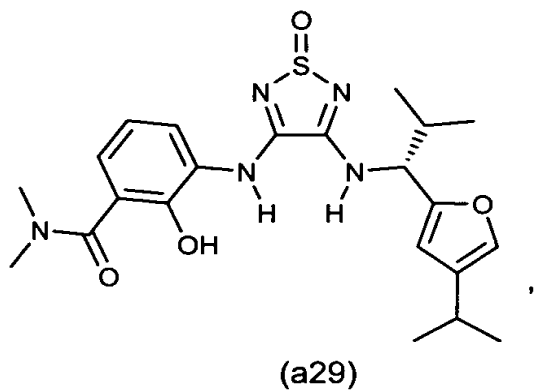


5

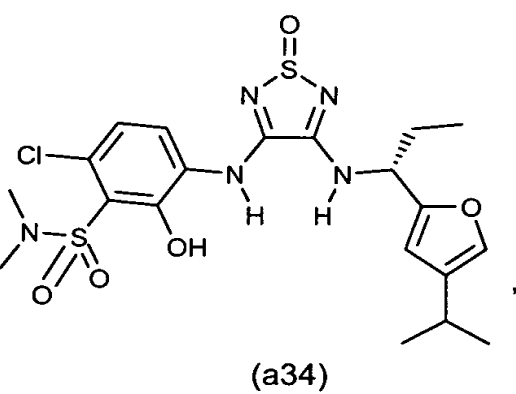
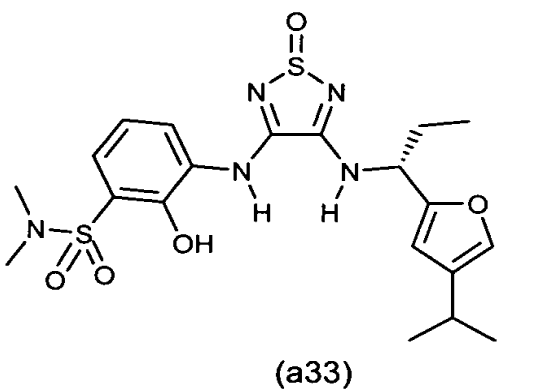
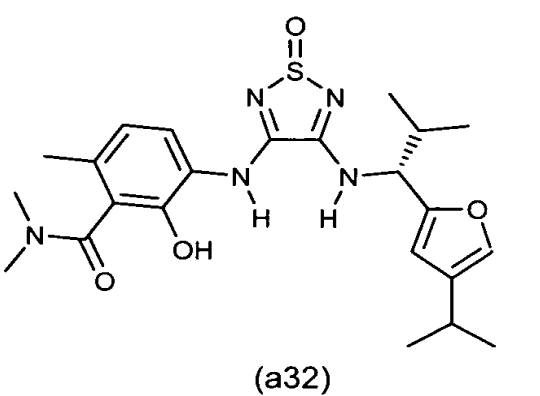
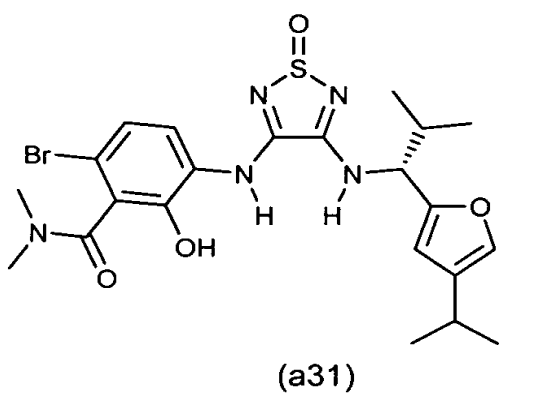


10



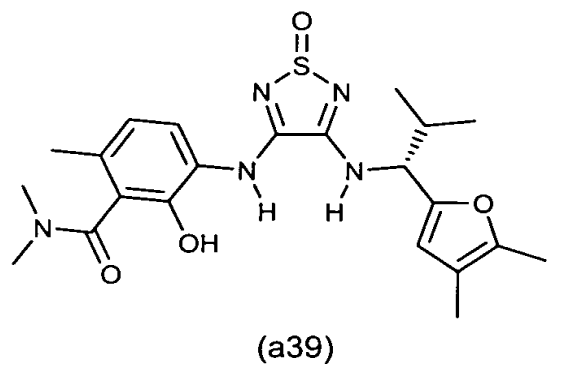
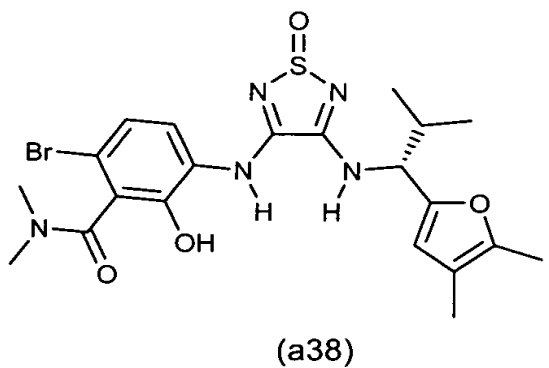
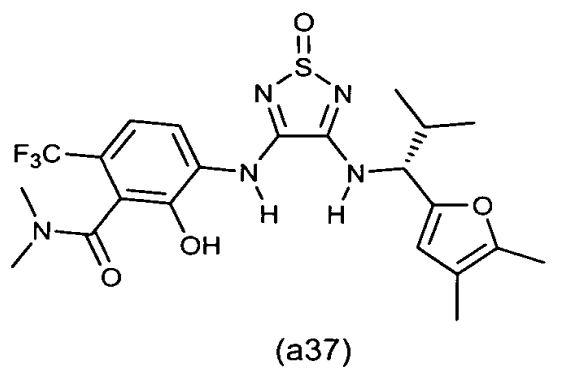
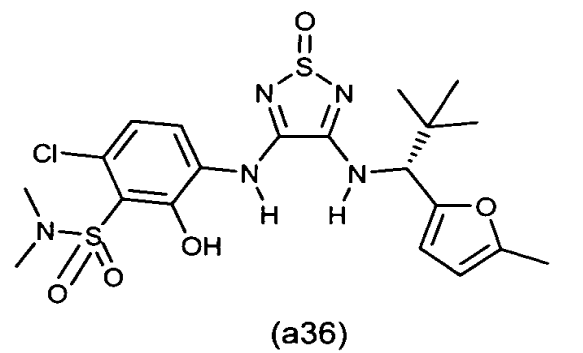
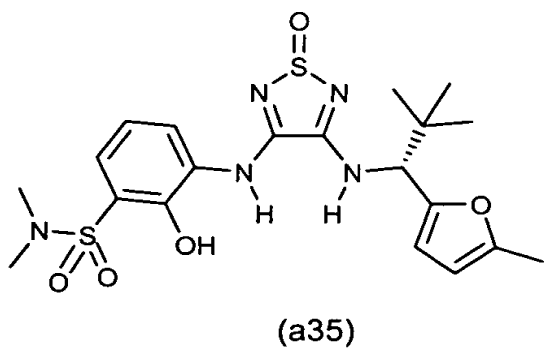


5



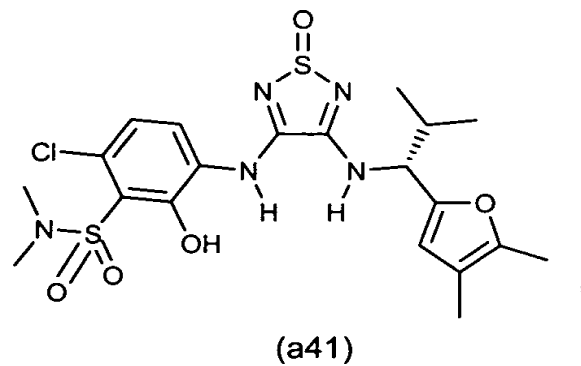
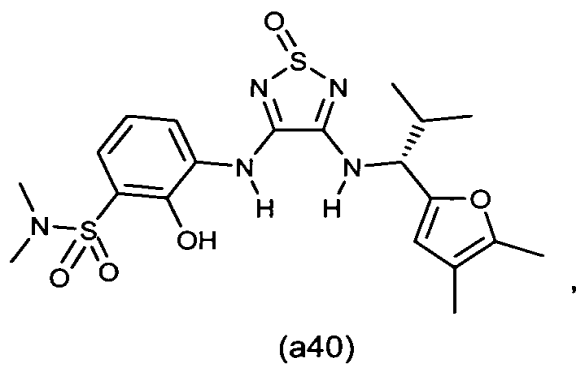
10



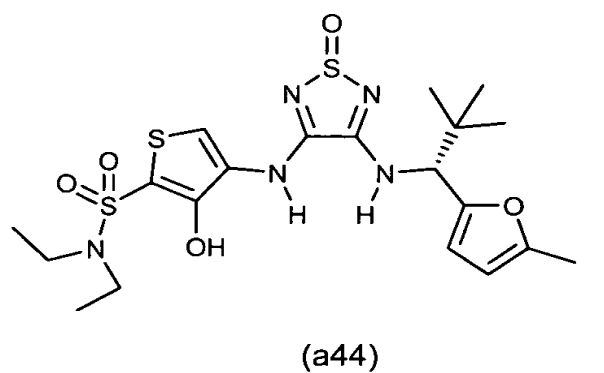
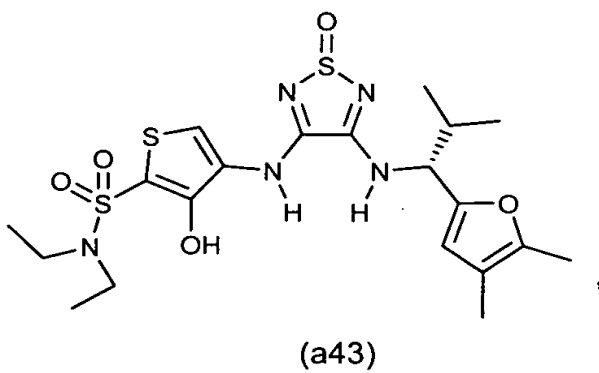
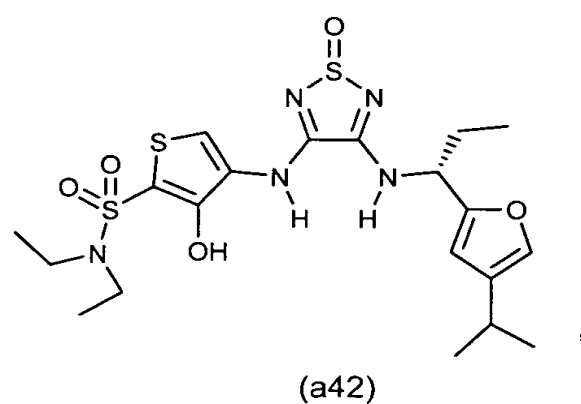
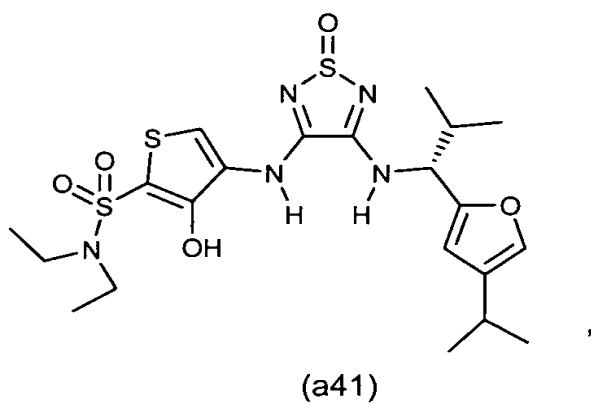


5

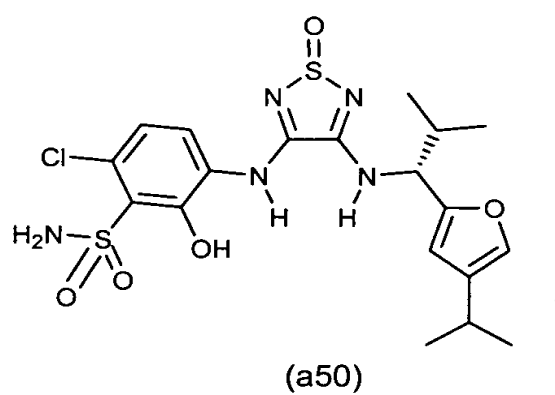
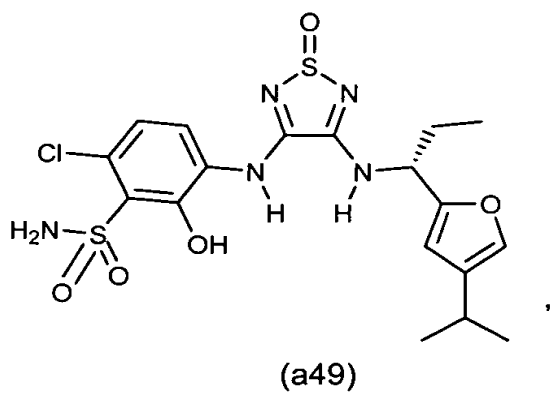
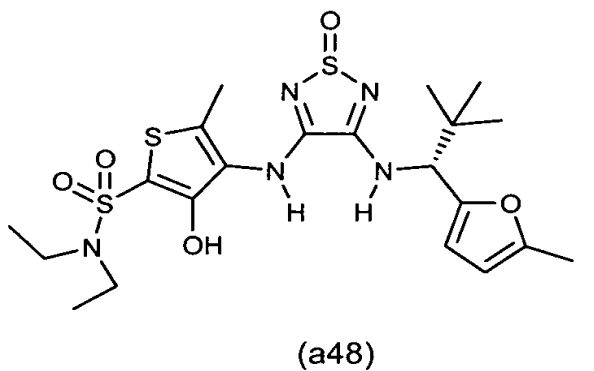
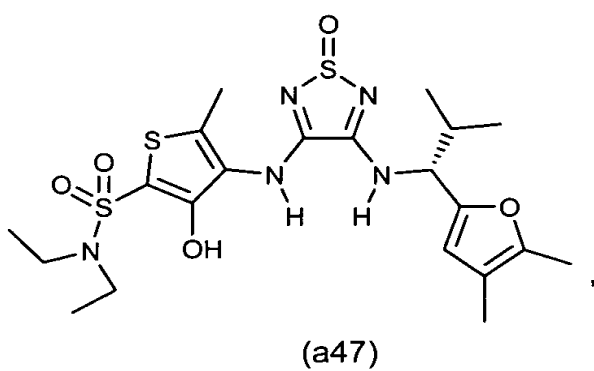
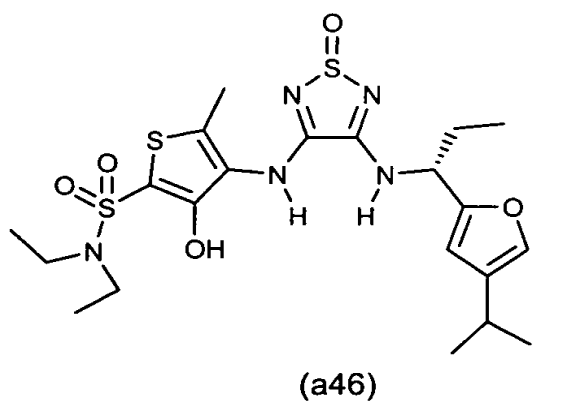
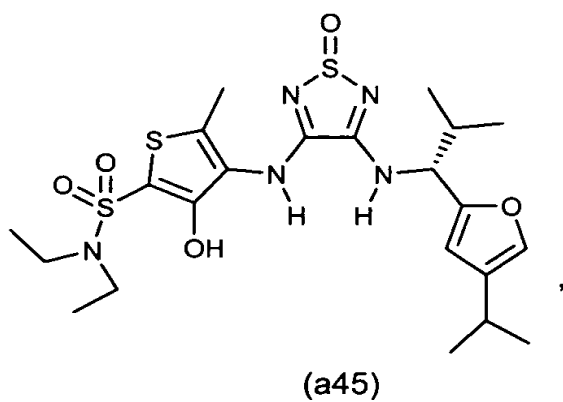
10

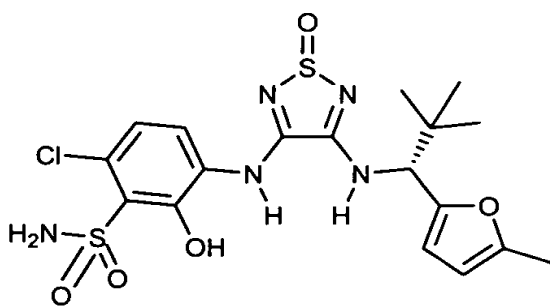


5



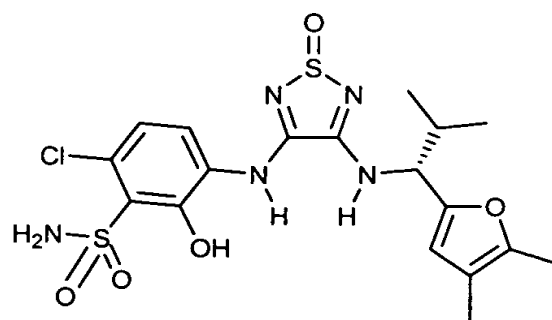
10





(a51)

and

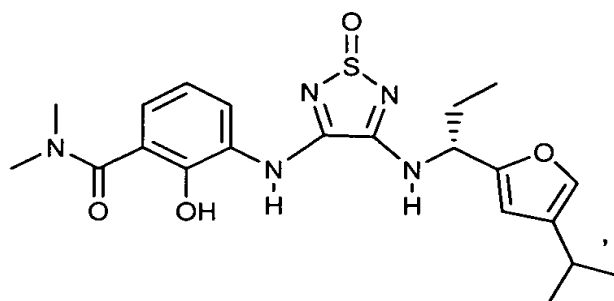


(a52)

pharmaceutically acceptable salts thereof, and pharmaceutically acceptable solvates thereof.

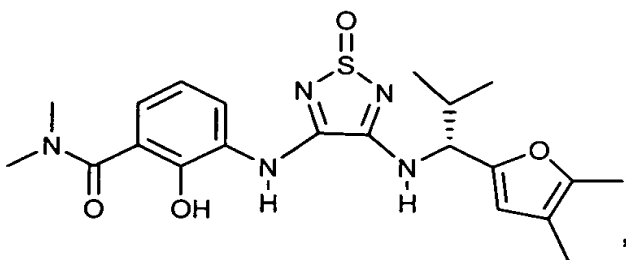
5

42. The compound of Claim 1 selected from the group consisting of compounds of the formula:

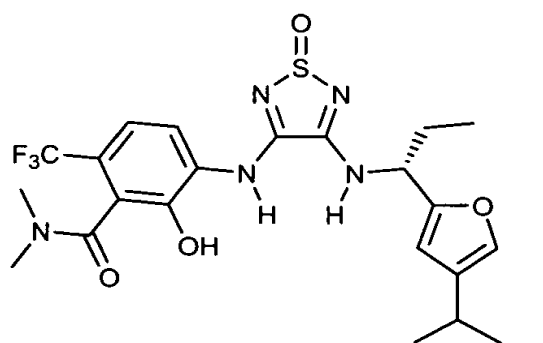


(a20)

10

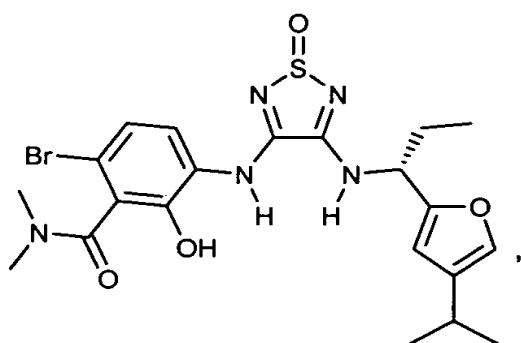


(a21)

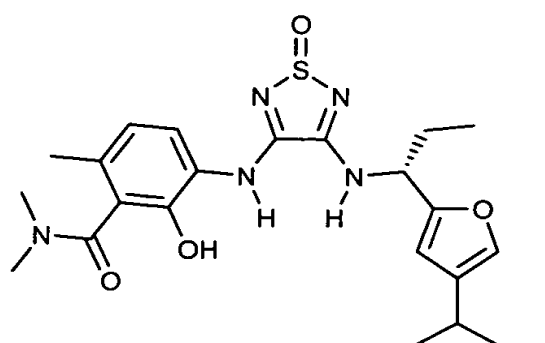


(a22)

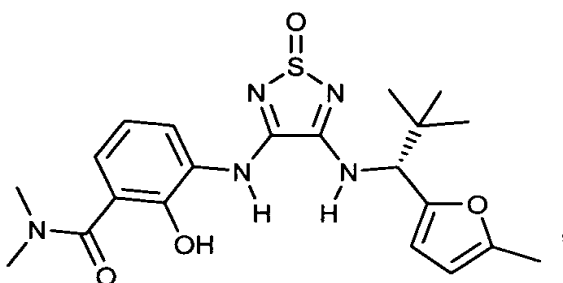
15



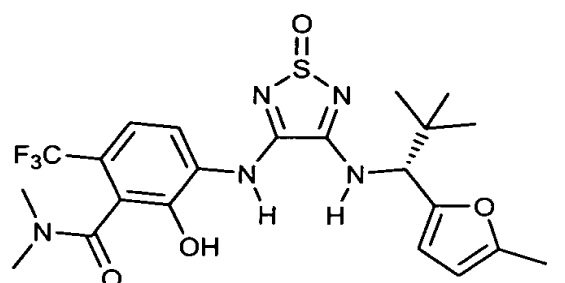
(a23)



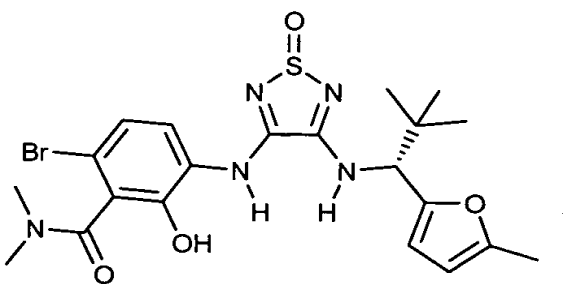
(a24)



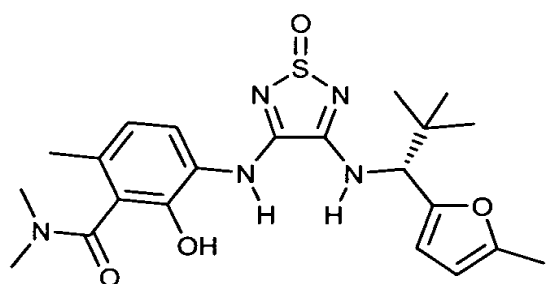
(a25)



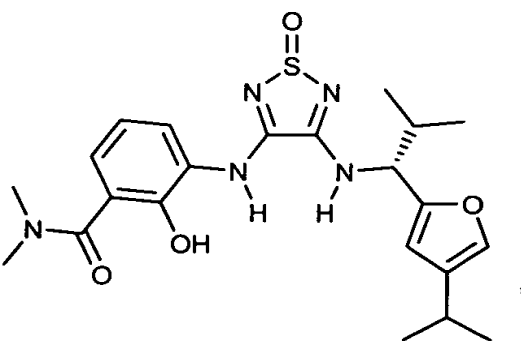
(a26)



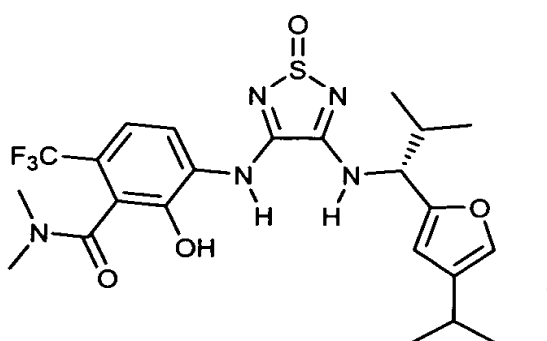
(a27)



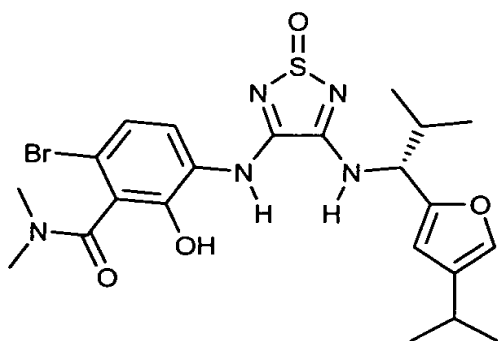
(a28)



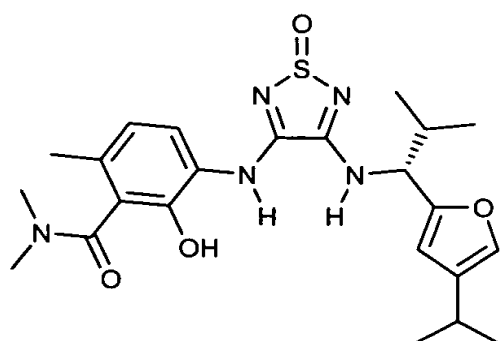
(a29)



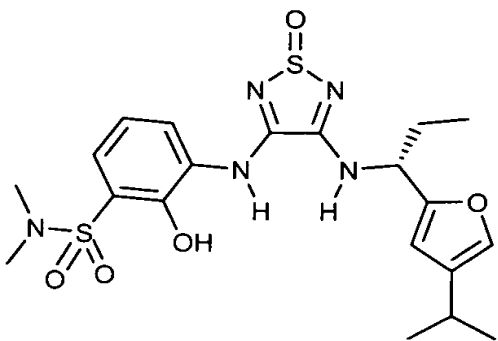
(a30)



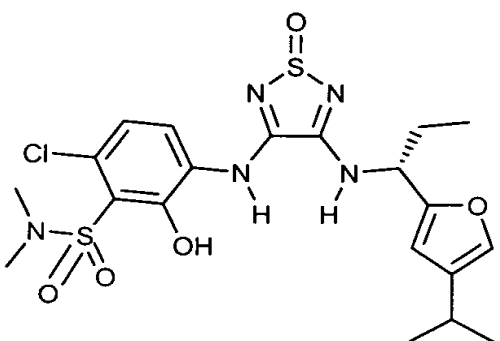
(a31)



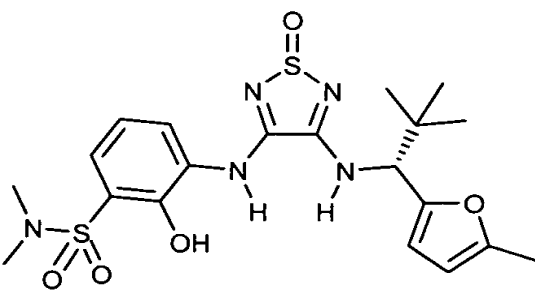
(a32)



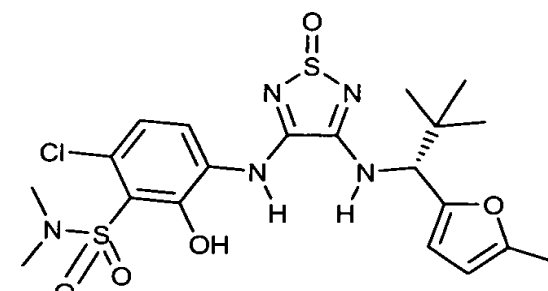
(a33)



(a34)



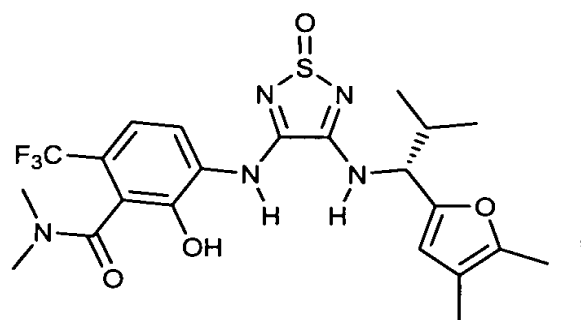
(a35)



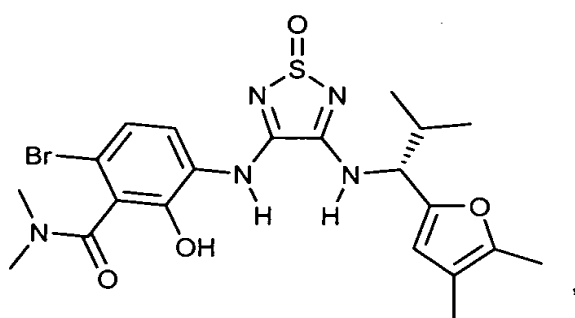
(a36)

5

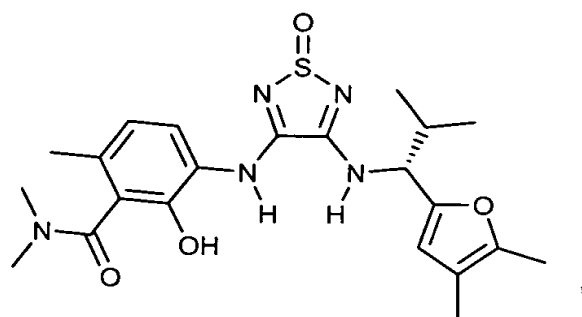
10



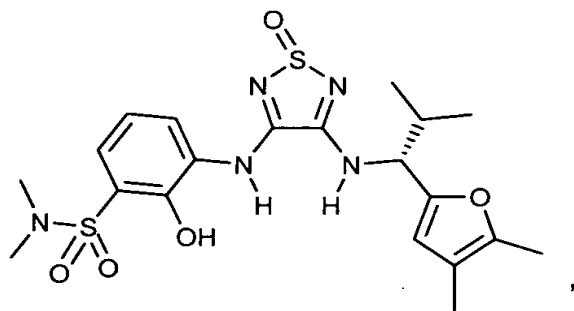
(a37)



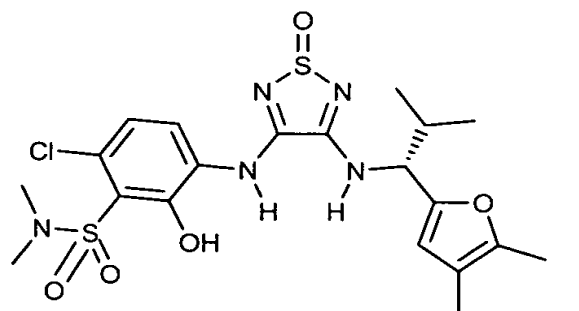
(a38)



(a39)



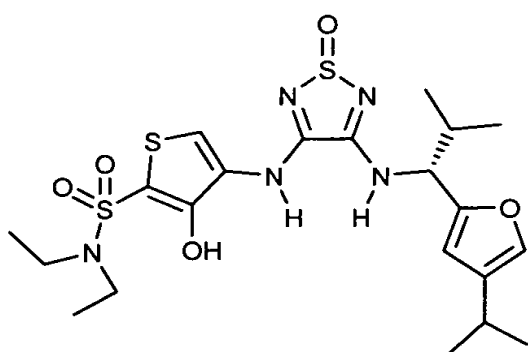
(a40)



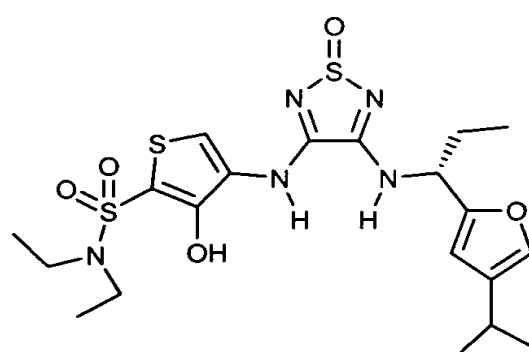
(a41)

5

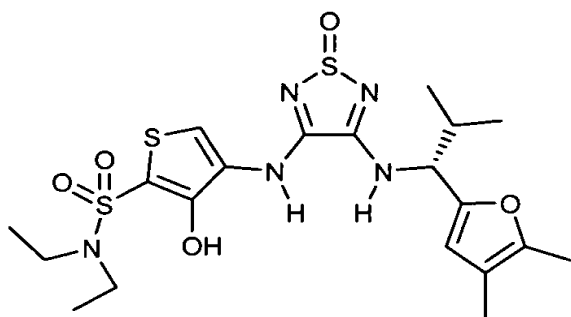
10



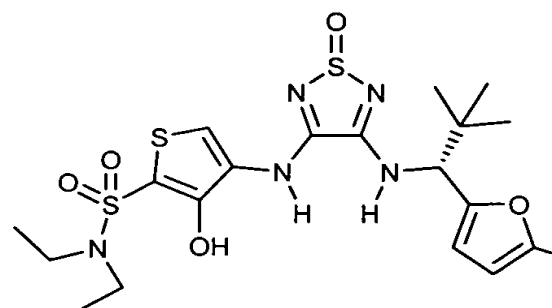
(a41)



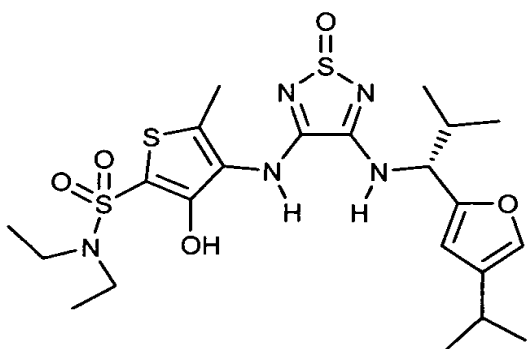
(a42)



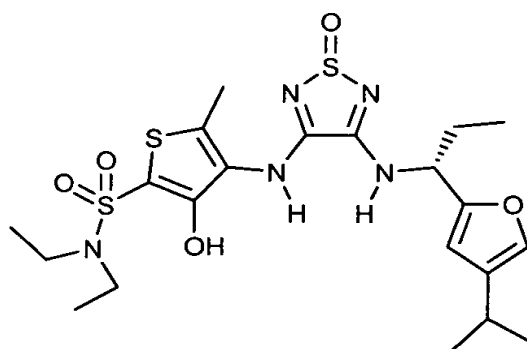
(a43)



(a44)

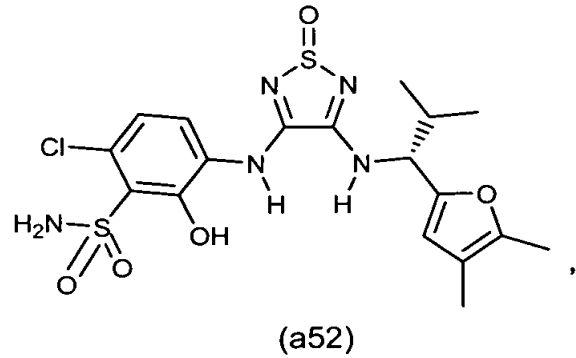
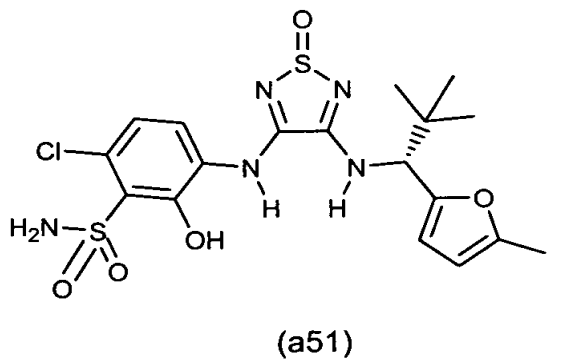
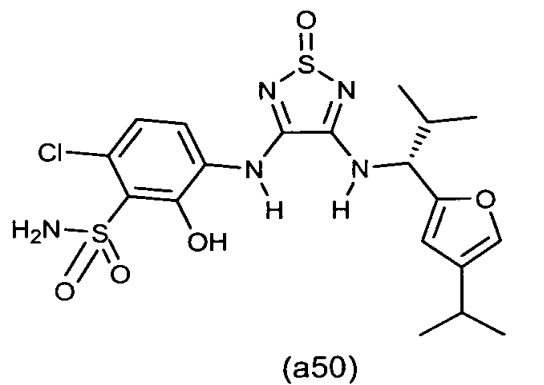
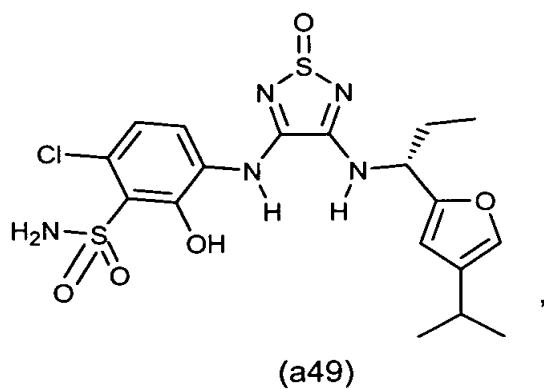
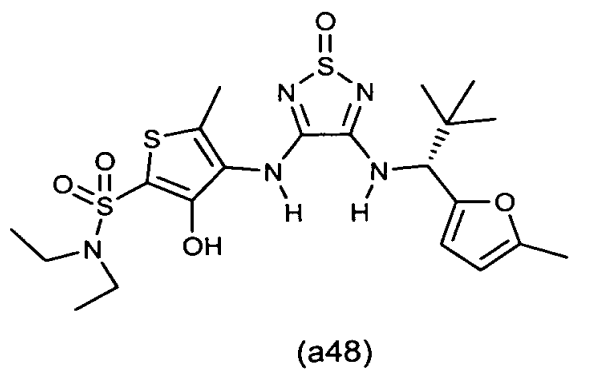
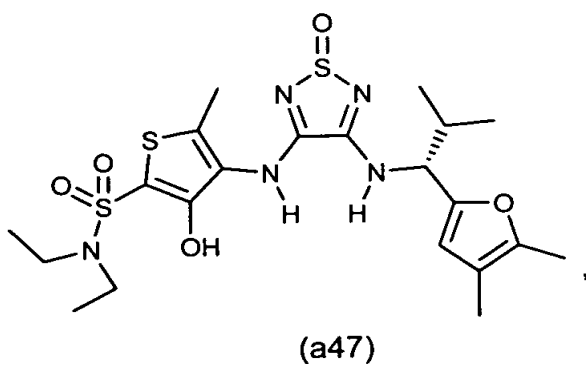


(a45)



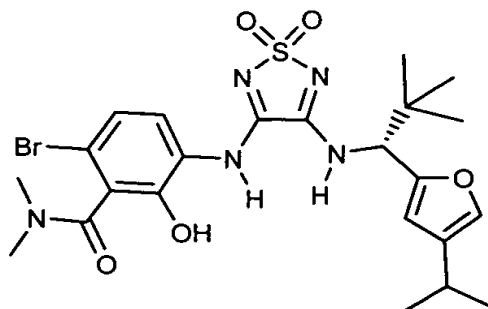
(a46)





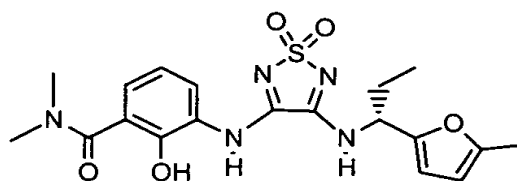
the pharmaceutically acceptable salts thereof, and the pharmaceutically acceptable solvates thereof.

43. The compound of Claim 41 having the formula:



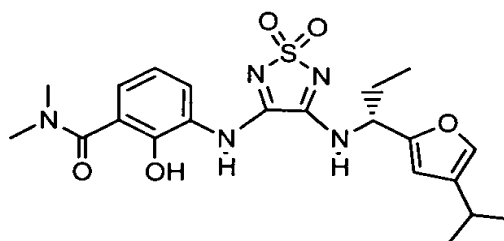
or a pharmaceutically acceptable salt or solvate thereof.

- 5 44. The compound of Claim 41 having the formula:



or a pharmaceutically acceptable salt or solvate thereof.

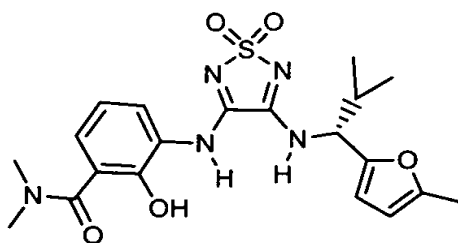
45. The compound of Claim 41 having the formula:



10

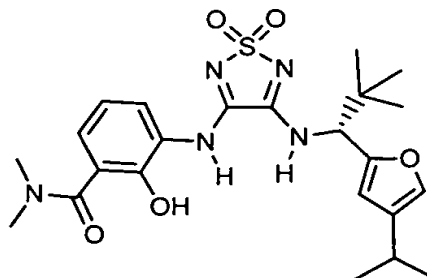
or a pharmaceutically acceptable salt or solvate thereof.

46. The compound of Claim 42 having the formula:



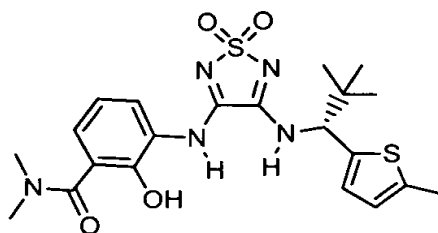
15 or a pharmaceutically acceptable salt or solvate thereof.

47. The compound of Claim 41 having the formula:



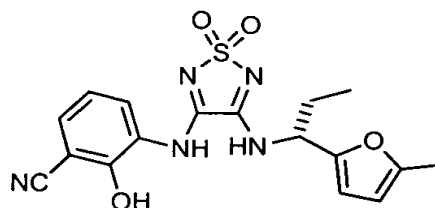
or a pharmaceutically acceptable salt or solvate thereof.

- 5 48. The compound of Claim 41 having the formula:



or a pharmaceutically acceptable salt or solvate thereof.

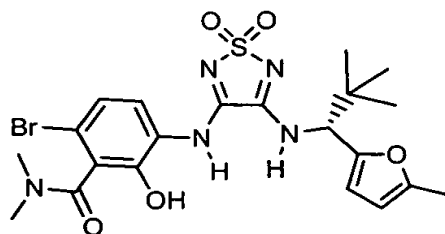
49. The compound of Claim 41 having the formula:



10

or a pharmaceutically acceptable salt or solvate thereof.

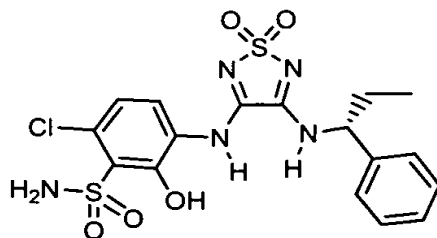
50. The compound of Claim 41 having the formula:



15

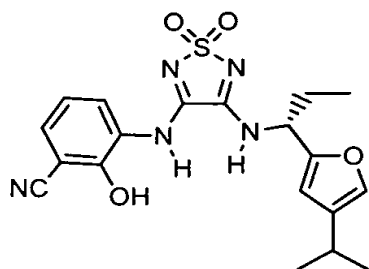
or a pharmaceutically acceptable salt or solvate thereof.

51. The compound of Claim 41 having the formula:



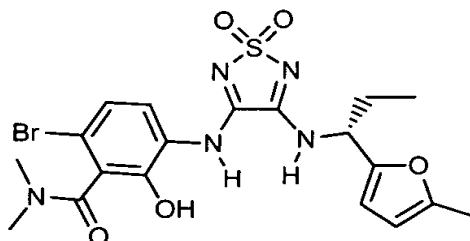
or a pharmaceutically acceptable salt or solvate thereof.

- 5 52. The compound of Claim 41 having the formula:



or a pharmaceutically acceptable salt or solvate thereof.

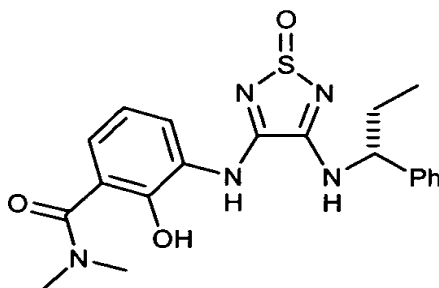
53. The compound of Claim 41 having the formula:



10

or a pharmaceutically acceptable salt or solvate thereof.

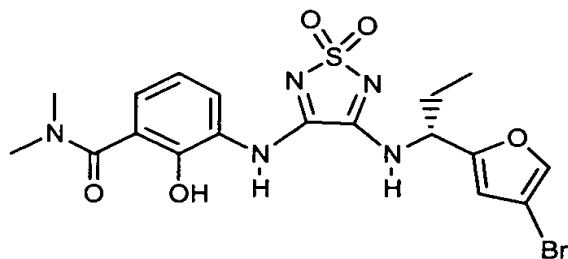
54. The compound of Claim 41 having the formula:



15

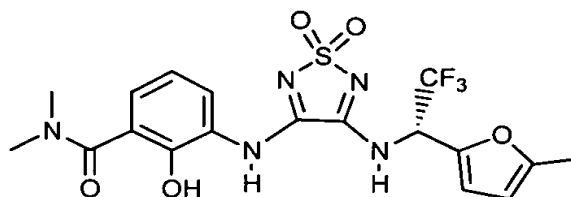
or a pharmaceutically acceptable salt or solvate thereof.

55. The compound of Claim 41 having the formula:



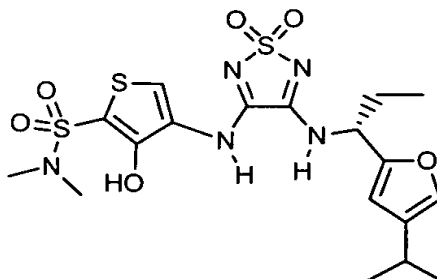
or a pharmaceutically acceptable salt or solvate thereof.

5 56. The compound of Claim 41 having the formula:



or a pharmaceutically acceptable salt or solvate thereof.

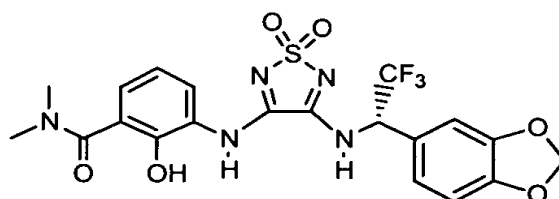
57. The compound of Claim 41 having the formula:



10

or a pharmaceutically acceptable salt or solvate thereof.

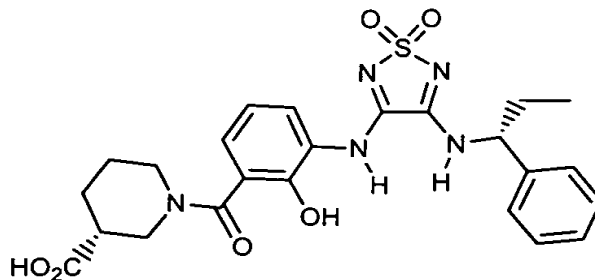
58. The compound of Claim 41 having the formula:



15

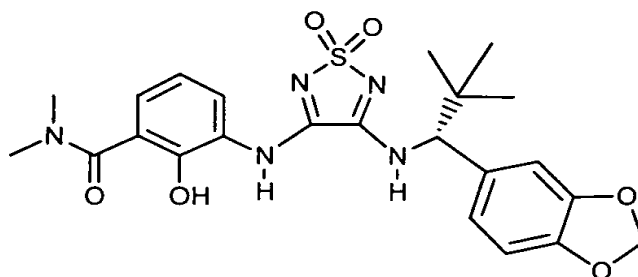
or a pharmaceutically acceptable salt or solvate thereof.

59. The compound of Claim 41 having the formula:



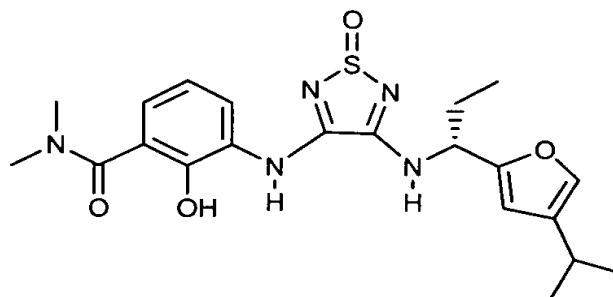
or a pharmaceutically acceptable salt or solvate thereof.

5 60. The compound of Claim 41 having the formula:



or a pharmaceutically acceptable salt or solvate thereof.

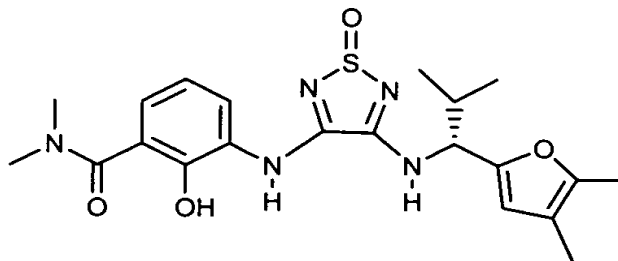
61. The compound of Claim 41 having the formula:



10

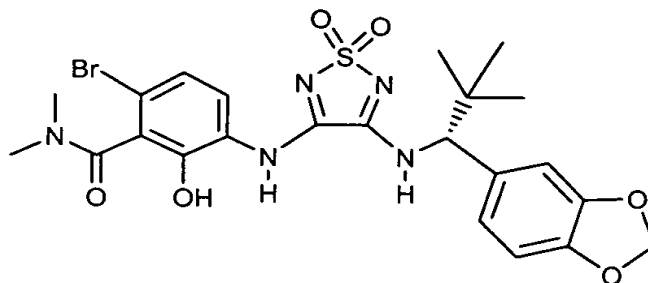
or a pharmaceutically acceptable salt or solvate thereof.

62. The compound of Claim 41 having the formula:



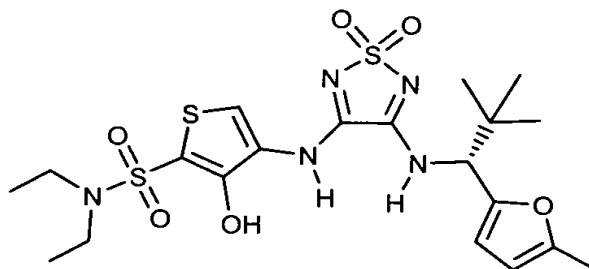
or a pharmaceutically acceptable salt or solvate thereof.

5 63. The compound of Claim 41 having the formula:



or a pharmaceutically acceptable salt or solvate thereof.

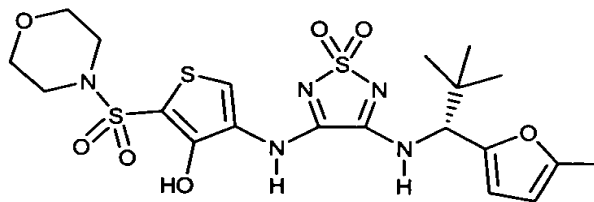
64. The compound of Claim 1 having the formula:



10

or a pharmaceutically acceptable salt or solvate thereof.

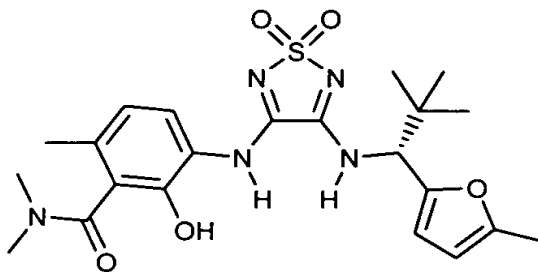
65. The compound of Claim 1 having the formula:



15

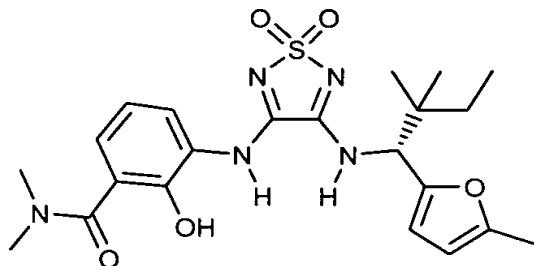
or a pharmaceutically acceptable salt or solvate thereof.

66. The compound of Claim 1 having the formula:



or a pharmaceutically acceptable salt or solvate thereof.

5 67. The compound of Claim 1 having the formula:



or a pharmaceutically acceptable salt or solvate thereof.

68. The compound of Claim 1 selected from the group consisting of the final  
10 compounds of Examples 1 to 201, 201A, 201.1 to 201.9, 202 to 204, 206 to 241,  
241.1, 241.2, 241.3, 241.4, 242 to 373 to 394, 2001 to 2060, and 2062 to 2113.

69. The compound of Claim 1 in isolated and pure form.

15 70. A pharmaceutical composition comprising at least one compound of  
Claim 1, or a pharmaceutically acceptable salt or solvate thereof, in combination with  
a pharmaceutically acceptable carrier.

20 71. A pharmaceutical composition comprising at least one compound of  
Claim 1, or a pharmaceutically acceptable salt or solvate thereof, and at least one  
other agent, medicament, antibody and/or inhibitor for treating a chemokine mediated  
disease, in combination with a pharmaceutically acceptable carrier.



72. A pharmaceutical composition comprising at least one compound of Claim 41, or a pharmaceutically acceptable salt or solvate thereof, in combination with a pharmaceutically acceptable carrier.

5           73. A pharmaceutical composition comprising at least one compound of Claim 41, or a pharmaceutically acceptable salt or solvate thereof, and at least one other agent, medicament, antibody and/or inhibitor for treating a chemokine mediated disease, in combination with a pharmaceutically acceptable carrier.

10           74. A method of treating a chemokine mediated diseases comprising administering to a patient in need of such treatment an effective amount of a compound of Claim 1, or a pharmaceutically acceptable salt or solvate thereof.

15           75. A method of treating cancer in a patient in need of such treatment comprising administering to said patient an effective amount of at least one compound of Claim 1, or a pharmaceutically acceptable salt or solvate thereof.

20           76. A method of treating cancer in a patient in need of such treatment comprising administering to said patient an effective amount of at least one compound of Claim 1, or a pharmaceutically acceptable salt or solvate thereof, in combination with at least one anticancer agent selected from the group consisting of: (a) microtubule affecting agents, (b) antineoplastic agents, (c) anti-angiogenesis agents, or (d) VEGF receptor kinase inhibitors, (e) antibodies against the VEGF receptor, (f) interferon, and g) radiation.

25           77. A method of treating cancer in a patient in need of such treatment comprising administering to said patient at least one compound of Claim 1, or a pharmaceutically acceptable salt or solvate thereof, in combination with at least one antineoplastic agent selected from the group consisting of: gemcitabine, paclitaxel, 5-  
30 Fluorouracil, cyclophosphamide, temozolomide, and Vincristine.

78. A method of treating cancer in a patient in need of such treatment, comprising administering to said patient an effective amount of at least one

compound of Claim 1, or a pharmaceutically acceptable salt or solvate thereof, concurrently or sequentially with a microtubule affecting agent.

79. A method treating cancer in a patient in need of such treatment comprising administering to said patient a therapeutically effective amount of: (a) at least one compound of Claim 1, or a pharmaceutically acceptable salt or solvate thereof, concurrently or sequentially with (b) at least one agent selected from the group consisting of: (1) antineoplastic agents, (2) microtubule affecting agents, and (3) anti-angiogenesis agents.

80. A method of inhibiting angiogenesis in a patient in need of such treatment comprising administering to said patient an effective amount of at least one compound of Claim 1, or a pharmaceutically acceptable salt or solvate thereof.

81. A method of treating angiogenic ocular disease in a patient in need of such treatment comprising administering to said patient an effective amount of at least one compound of Claim 1, or a pharmaceutically acceptable salt or solvate thereof.

82. A method of treating a disease selected from the group consisting of: acute pain, acute inflammation, chronic inflammation, rheumatoid arthritis, acute inflammatory pain, chronic inflammatory pain, neuropathic pain, psoriasis, atopic dermatitis, asthma, COPD, adult respiratory disease, arthritis, inflammatory bowel disease, Crohn's disease, ulcerative colitis, septic shock, endotoxic shock, gram negative sepsis, toxic shock syndrome, stroke, cardiac reperfusion injury, renal reperfusion injury, glomerulonephritis, thrombosis, Alzheimer's disease, graft vs. host reaction, allograft rejections, malaria, acute respiratory distress syndrome, delayed type hypersensitivity reaction, atherosclerosis, cerebral ischemia, cardiac ischemia, osteoarthritis, multiple sclerosis, restinosis, angiogenesis, osteoporosis, gingivitis, respiratory viruses, herpes viruses, hepatitis viruses, HIV, Kaposi's sarcoma associated virus, meningitis, cystic fibrosis, pre-term labor, cough, pruritis, multi-organ dysfunction, trauma, strains, sprains, contusions, psoriatic arthritis, herpes, encephalitis, CNS vasculitis, traumatic brain injury, CNS tumors, subarachnoid hemorrhage, post surgical trauma, interstitial pneumonitis, hypersensitivity, crystal

induced arthritis, acute pancreatitis, chronic pancreatitis, acute alcoholic hepatitis, necrotizing enterocolitis, chronic sinusitis, angiogenic ocular disease, ocular inflammation, retinopathy of prematurity, diabetic retinopathy, macular degeneration with the wet type preferred, corneal neovascularization, polymyositis, vasculitis, acne, 5 gastric ulcers, duodenal ulcers, celiac disease, esophagitis, glossitis, airflow obstruction, airway hyperresponsiveness, bronchiectasis, bronchiolitis, bronchiolitis obliterans, chronic bronchitis, cor pulmonae, dyspnea, emphysema, hypercapnea, hyperinflation, hypoxemia, hyperoxia-induced inflammations, hypoxia, surgical lung volume reduction, pulmonary fibrosis, pulmonary hypertension, right ventricular 10 hypertrophy, peritonitis associated with continuous ambulatory peritoneal dialysis (CAPD), granulocytic ehrlichiosis, sarcoidosis, small airway disease, ventilation-perfusion mismatching, wheeze, colds, gout, alcoholic liver disease, lupus, burn therapy, periodontitis, cancer, transplant reperfusion injury, early transplantation rejection, airway hyperreactivity, allergic contact dermatitis, allergic rhinitis, alopecia 15 areata, antiphospholipid syndromes, aplastic anemia, autoimmune deafness, autoimmune hemolytic syndromes, autoimmune hepatitis, autoimmune neuropathy, autoimmune ovarian failure, autoimmune orchitis, autoimmune thrombocytopenia, bullous pemphigoid, chronic allograft vasculopathy, chronic inflammatory demyelinating polyneuropathy, cirrhosis, cor pneumoniae, cryoglobulinemia, 20 dermatomyositis, diabetes, drug-induced autoimmunity, epidermolysis bullosa acquisita, endometriosis, fibrotic diseases, gastritis, Goodpasture's syndrome, Graves' disease, Guillain-Barre disease, Hashimoto's thyroiditis, hepatitis-associated autoimmunity, HIV-related autoimmune syndromes and hematologic disorders, hypophytis, idiopathic thrombocytic pupura, interstitial cystitis, juvenile arthritis, 25 Langerhans' cell histiocytitis, lichen planus, metal-induced autoimmunity, myasthenia gravis, myelodysplastic syndromes, myocarditis, myositis, Neuropathies, nephritic syndrome, optic neuritis, pancreatitis, paroxysmal nocturnal hemoglobinemia, pemphigus, polymyalgia, post-infectious autoimmunity, primary biliary cirrhosis, reactive arthritis, ankylosing spondylitis, Raynaud's phenomenon, Reiter's syndrome, 30 reperfusion injury, scleritis, scleroderma, secondary hematologic manifestation of autoimmune diseases, silicone implant associated autoimmune disease, Sjogren's syndrome, systemic lupus erythematosus, thrombocytopenia, transverse myelitis, tubulointerstitial nephritis, uveitis, vasculitis syndromes, and Vitiligo in a patient in need of such treatment comprising administering to said patient an effective amount

of at least one compound of Claim 1, or a pharmaceutically acceptable salt or solvate thereof.

83. A method of treating a chemokine mediated disease in a patient in need of such treatment comprising administering to said patient at least one compound of Claim 1, or a pharmaceutically acceptable salt or solvate thereof, in combination with at least one other medicament useful for the treatment of chemokine mediated diseases.

84. A method of treating a chemokine mediated disease in a patient in need of such treatment comprising administering to said patient at least one compound of Claim 1, or a pharmaceutically acceptable salt or solvate thereof, in combination with at least one other medicament selected from the group consisting of:

- a) disease modifying antirheumatic drugs;
- b) nonsteroidal anitnflammatory drugs;
- c) COX-2 selective inhibitors;
- d) COX-1 inhibitors;
- e) immunosuppressives;
- f) steroids;
- g) biological response modifiers; and
- h) other anti-inflammatory agents or therapeutics useful for the treatment of chemokine mediated diseases.

85. A method of treating a pulmonary disease in a patient in need of such treatment, comprising administering to said patient a therapeutically effective amount of at least one compound of Claim 1, or a pharmaceutically acceptable salt or solvate thereof, in combination with at least one compound selected from the group consisting of: glucocorticoids, 5-lipoxygenase inhibitors,  $\beta$ -2 adrenoceptor agonists, muscarinic M1 antagonists, muscarinic M3 antagonists, muscarinic M2 agonists, NK3 antagonists, LTB4 antagonists, cysteinyl leukotriene antagonists, bronchodilators, PDE4 inhibitors, PDE inhibitors, elastase inhibitors, MMP inhibitors, phospholipase A2 inhibitors, phospholipase D inhibitors, histamine H1 antagonists, histamine H3 antagonists, dopamine agonists, adenosine A2 agonists, NK1 and NK2 antagonists,

GABA-b agonists, nociceptin agonists, expectorants, mucolytic agents, decongestants, antioxidants, anti-IL-8 anti-bodies, anti-IL-5 antibodies, anti-IgE antibodies, anti-TNF antibodies, IL-10, adhesion molecule inhibitors, and growth hormones.

5

86. A method of treating multiple sclerosis in a patient in need of such treatment comprising administering to said patient a therapeutically effective amount of at least one compound of Claim 1, or a pharmaceutically acceptable salt or solvate thereof, in combination with at least one compound selected from the group  
10 consisting of glatiramer acetate, glucocorticoids, methotrexate, azothioprine, mitoxantrone, chemokine inhibitors, and CB2-selective inhibitors.

87. A method of treating multiple sclerosis in a patient in need of such treatment comprising administering to said patient a therapeutically effective amount  
15 of at least one compound of Claim 1, or a pharmaceutically acceptable salt or solvate thereof, in combination with at least one compound selected from the group consisting of: methotrexate, cyclosporin, leflunimide, sulfasalazine,  $\beta$ -methasone,  $\beta$ -interferon, glatiramer acetate, prednisone, etonercept, and infliximab.

20 88. A method of treating rheumatoid arthritis in a patient in need of such treatment comprising administering to said patient a therapeutically effective amount of at least one compound of Claim 1, or a pharmaceutically acceptable salt or solvate thereof.

89. A method of treating rheumatoid arthritis in a patient in need of such treatment comprising administering to said patient a therapeutically effective amount of at least one compound of Claim 1, or a pharmaceutically acceptable salt or solvate thereof, in combination with at least one compound selected from the group consisting of COX-2 inhibitors, COX inhibitors, immunosuppressives, steroids, PDE IV inhibitors, anti-TNF- $\alpha$  compounds, MMP inhibitors, glucocorticoids, chemokine inhibitors, CB2-selective inhibitors, and other classes of compounds indicated for the treatment of rheumatoid arthritis.

90. A method of treating stroke and cardiac reperfusion injury in a patient in need of such treatment comprising administering to said patient a therapeutically effective amount of at least one compound of Claim 1, or a pharmaceutically acceptable salt or solvate thereof, in combination with at least one compound selected from the group consisting of thrombolitics, antiplatelet agents, antagonists, anticoagulants, and other compounds indicated for the treatment of rheumatoid arthritis.

91. A method of treating stroke and cardiac reperfusion injury in a patient in need of such treatment comprising administering to said patient a therapeutically effective amount of at least one compound of Claim 1, or a pharmaceutically acceptable salt or solvate thereof, in combination with at least one compound selected from the group consisting of tenecteplase, TPA, alteplase, abciximab, eptifibatide, and heparin.

92. A method of treating psoriasis in a patient in need of such treatment, comprising administering to said patient a therapeutically effective amount of at least one compound of Claim 1, or a pharmaceutically acceptable salt or solvate thereof, in combination with at least one compound selected from the group consisting of immunosuppressives, steroids, and anti-TNF- $\alpha$  compounds.

93. A method of treating COPD in a patient in need of such treatment, comprising administering to said patient a therapeutically effective amount of at least one compound of Claim 1, or a pharmaceutically acceptable salt or solvate thereof.

5           94. A method of treating acute pain in a patient in need of such treatment, comprising administering to said patient a therapeutically effective amount of at least one compound of Claim 1, or a pharmaceutically acceptable salt or solvate thereof.

10           95. A method of treating acute inflammatory pain in a patient in need of such treatment, comprising administering to said patient a therapeutically effective amount of at least one compound of Claim 1, or a pharmaceutically acceptable salt or solvate thereof.

15           96. A method of treating chronic inflammatory pain in a patient in need of such treatment, comprising administering to said patient a therapeutically effective amount of at least one compound of Claim 1, or a pharmaceutically acceptable salt or solvate thereof.

20           97. A method of treating neuropathic pain in a patient in need of such treatment, comprising administering to said patient a therapeutically effective amount of at least one compound of Claim 1, or a pharmaceutically acceptable salt or solvate thereof.

25           98. A method of treating arthritis in a patient in need of such treatment, comprising administering to said patient a therapeutically effective amount of at least one compound of Claim 1, or a pharmaceutically acceptable salt or solvate thereof.

30           99. A method of treating osteoarthritis in a patient in need of such treatment, comprising administering to said patient a therapeutically effective amount of at least one compound of Claim 1, or a pharmaceutically acceptable salt or solvate thereof.

100. A method of treating a chemokine mediated diseases comprising administering to a patient in need of such treatment an effective amount of a compound of Claim 41, or a pharmaceutically acceptable salt or solvate thereof.

5           101. A method of treating cancer in a patient in need of such treatment comprising administering to said patient an effective amount of at least one compound of Claim 41, or a pharmaceutically acceptable salt or solvate thereof.

10           102. A method of treating cancer in a patient in need of such treatment comprising administering to said patient an effective amount of at least one compound of Claim 41, or a pharmaceutically acceptable salt or solvate thereof, in combination with at least one anticancer agent selected from the group consisting of: (a) microtubule affecting agents, (b) antineoplastic agents, (c) anti-angiogenesis agents, or (d) VEGF receptor kinase inhibitors, (e) antibodies against the VEGF  
15           receptor, (f) interferon, and g) radiation.

            103. A method of treating cancer in a patient in need of such treatment comprising administering to said patient at least one compound of Claim 41, or a pharmaceutically acceptable salt or solvate thereof, in combination with at least one  
20           antineoplastic agent selected from the group consisting of: gemcitabine, paclitaxel, 5-Fluorouracil, cyclophosphamide, temozolomide, and Vincristine.

            104. A method of treating cancer in a patient in need of such treatment, comprising administering to said patient an effective amount of at least one  
25           compound of Claim 41, or a pharmaceutically acceptable salt or solvate thereof, concurrently or sequentially with a microtubule affecting agent.

            105. A method treating cancer in a patient in need of such treatment comprising administering to said patient a therapeutically effective amount of: (a) at  
30           least one compound of Claim 41, or a pharmaceutically acceptable salt or solvate thereof, concurrently or sequentially with (b) at least one agent selected from the group consisting of: (1) antineoplastic agents, (2) microtubule affecting agents, and (3) anti-angiogenesis agents.



106. A method of inhibiting angiogenesis in a patient in need of such treatment comprising administering to said patient an effective amount of at least one compound of Claim 41, or a pharmaceutically acceptable salt or solvate thereof.

5           107. A method of treating angiogenic ocular disease in a patient in need of such treatment comprising administering to said patient an effective amount of at least one compound of Claim 41, or a pharmaceutically acceptable salt or solvate thereof.

10           108. A method of treating a disease selected from the group consisting of:  
acute pain, acute inflammation, chronic inflammation, rheumatoid arthritis, acute  
inflammatory pain, chronic inflammatory pain, neuropathic pain, psoriasis, atopic  
dermatitis, asthma, COPD, adult respiratory disease, arthritis, inflammatory bowel  
disease, Crohn's disease, ulcerative colitis, septic shock, endotoxic shock, gram  
15 negative sepsis, toxic shock syndrome, stroke, cardiac reperfusion injury, renal  
reperfusion injury, glomerulonephritis, thrombosis, Alzheimer's disease, graft vs. host  
reaction, allograft rejections, malaria, acute respiratory distress syndrome, delayed  
type hypersensitivity reaction, atherosclerosis, cerebral ischemia, cardiac ischemia,  
osteoarthritis, multiple sclerosis, restinosis, angiogenesis, osteoporosis, gingivitis,  
20 respiratory viruses, herpes viruses, hepatitis viruses, HIV, Kaposi's sarcoma  
associated virus, meningitis, cystic fibrosis, pre-term labor, cough, pruritis, multi-organ  
dysfunction, trauma, strains, sprains, contusions, psoriatic arthritis, herpes,  
encephalitis, CNS vasculitis, traumatic brain injury, CNS tumors, subarachnoid  
hemorrhage, post surgical trauma, interstitial pneumonitis, hypersensitivity, crystal  
25 induced arthritis, acute pancreatitis, chronic pancreatitis, acute alcoholic hepatitis,  
necrotizing enterocolitis, chronic sinusitis, angiogenic ocular disease, ocular  
inflammation, retinopathy of prematurity, diabetic retinopathy, macular degeneration  
with the wet type preferred, corneal neovascularization, polymyositis, vasculitis, acne,  
gastric ulcers, duodenal ulcers, celiac disease, esophagitis, glossitis, airflow  
30 obstruction, airway hyperresponsiveness, bronchiectasis, bronchiolitis, bronchiolitis  
obliterans, chronic bronchitis, cor pulmonae, dyspnea, emphysema, hypercapnea,  
hyperinflation, hypoxemia, hyperoxia-induced inflammations, hypoxia, surgical lung  
volume reduction, pulmonary fibrosis, pulmonary hypertension, right ventricular  
hypertrophy, peritonitis associated with continuous ambulatory peritoneal dialysis

(CAPD), granulocytic ehrlichiosis, sarcoidosis, small airway disease, ventilation-perfusion mismatching, wheeze, colds, gout, alcoholic liver disease, lupus, burn therapy, periodontitis, cancer, transplant reperfusion injury, early transplantation rejection, airway hyperreactivity, allergic contact dermatitis, allergic rhinitis, alopecia areata, antiphospholipid syndromes, aplastic anemia, autoimmune deafness, autoimmune hemolytic syndromes, autoimmune hepatitis, autoimmune neuropathy, autoimmune ovarian failure, autoimmune orchitis, autoimmune thrombocytopenia, bullous pemphigoid, chronic allograft vasculopathy, chronic inflammatory demyelinating polyneuropathy, cirrhosis, cor pulmonariae, cryoglobulinemia, dermatomyositis, diabetes, drug-induced autoimmunity, epidermolysis bullosa acquisita, endometriosis, fibrotic diseases, gastritis, Goodpasture's syndrome, Graves' disease, Guillain-Barre disease, Hashimoto's thyroiditis, hepatitis-associated autoimmunity, HIV-related autoimmune syndromes and hematologic disorders, hypophytis, idiopathic thrombocytic purpura, interstitial cystitis, juvenile arthritis, Langerhans' cell histiocytitis, lichen planus, metal-induced autoimmunity, myasthenia gravis, myelodysplastic syndromes, myocarditis, myositis, Neuropathies, nephritic syndrome, optic neuritis, pancreatitis, paroxysmal nocturnal hemoglobinemia, pemphigus, polymyalgia, post-infectious autoimmunity, primary biliary cirrhosis, reactive arthritis, ankylosing spondylitis, Raynaud's phenomenon, Reiter's syndrome, reperfusion injury, scleritis, scleroderma, secondary hematologic manifestation of autoimmune diseases, silicone implant associated autoimmune disease, Sjogren's syndrome, systemic lupus erythematosus, thrombocytopenia, transverse myelitis, tubulointerstitial nephritis, uveitis, vasculitis syndromes, and Vitiligo in a patient in need of such treatment comprising administering to said patient an effective amount of at least one compound of Claim 41, or a pharmaceutically acceptable salt or solvate thereof.

109. A method of treating a chemokine mediated disease in a patient in need of such treatment comprising administering to said patient at least one compound of Claim 41, or a pharmaceutically acceptable salt or solvate thereof, in combination with at least one other medicament useful for the treatment of chemokine mediated diseases.

110. A method of treating a chemokine mediated disease in a patient in need of such treatment comprising administering to said patient at least one compound of Claim 41, or a pharmaceutically acceptable salt or solvate thereof, in combination with at least one other medicament selected from the group consisting of:

- a) disease modifying antirheumatic drugs;
- b) nonsteroidal anitnflammatory drugs;
- c) COX-2 selective inhibitors;
- d) COX-1 inhibitors;
- e) immunosuppressives;
- f) steroids;
- g) biological response modifiers; and
- h) other anti-inflammatory agents or therapeutics useful for the treatment of chemokine mediated diseases.

111. A method of treating a pulmonary disease in a patient in need of such treatment, comprising administering to said patient a therapeutically effective amount of at least one compound of Claim 41, or a pharmaceutically acceptable salt or solvate thereof, in combination with at least one compound selected from the group consisting of: glucocorticoids, 5-lipoxygenase inhibitors,  $\beta$ -2 adrenoceptor agonists, muscarinic M1 antagonists, muscarinic M3 antagonists, muscarinic M2 agonists, NK3 antagonists, LTB4 antagonists, cysteinyl leukotriene antagonists, bronchodilators, PDE4 inhibitors, PDE inhibitors, elastase inhibitors, MMP inhibitors, phospholipase A2 inhibitors, phospholipase D inhibitors, histamine H1 antagonists, histamine H3 antagonists, dopamine agonists, adenosine A2 agonists, NK1 and NK2 antagonists, GABA-b agonists, nociceptin agonists, expectorants, mucolytic agents, decongestants, antioxidants, anti-IL-8 anti-bodies, anti-IL-5 antibodies, anti-IgE antibodies, anti-TNF antibodies, IL-10, adhesion molecule inhibitors, and growth hormones.

112. A method of treating multiple sclerosis in a patient in need of such treatment comprising administering to said patient a therapeutically effective amount of at least one compound of Claim 41, or a pharmaceutically acceptable salt or solvate thereof, in combination with at least one compound selected from the group

consisting of glatiramer acetate, glucocorticoids, methotrexate, azothioprine, mitoxantrone, chemokine inhibitors, and CB2-selective inhibitors.

113. A method of treating multiple sclerosis in a patient in need of such treatment comprising administering to said patient a therapeutically effective amount of at least one compound of Claim 41, or a pharmaceutically acceptable salt or solvate thereof, in combination with at least one compound selected from the group consisting of: methotrexate, cyclosporin, leflunimide, sulfasalazine,  $\beta$ -methasone,  $\beta$ -interferon, glatiramer acetate, prednisone, etonercept, and infliximab.

114. A method of treating rheumatoid arthritis in a patient in need of such treatment comprising administering to said patient a therapeutically effective amount of at least one compound of Claim 41, or a pharmaceutically acceptable salt or solvate thereof.

115. A method of treating rheumatoid arthritis in a patient in need of such treatment comprising administering to said patient a therapeutically effective amount of at least one compound of Claim 41, or a pharmaceutically acceptable salt or solvate thereof, in combination with at least one compound selected from the group consisting of COX-2 inhibitors, COX inhibitors, immunosuppressives, steroids, PDE IV inhibitors, anti-TNF- $\alpha$  compounds, MMP inhibitors, glucocorticoids, chemokine inhibitors, CB2-selective inhibitors, and other classes of compounds indicated for the treatment of rheumatoid arthritis.

116. A method of treating stroke and cardiac reperfusion injury in a patient in need of such treatment comprising administering to said patient a therapeutically effective amount of at least one compound of Claim 41, or a pharmaceutically acceptable salt or solvate thereof, in combination with at least one compound selected from the group consisting of thrombolitics, antiplatelet agents, antagonists, anticoagulants, and other compounds indicated for the treatment of rheumatoid arthritis.

117. A method of treating stroke and cardiac reperfusion injury in a patient in need of such treatment comprising administering to said patient a therapeutically effective amount of at least one compound of Claim 41, or a pharmaceutically acceptable salt or solvate thereof, in combination with at least one compound selected from the group consisting of tenecteplase, TPA, alteplase, abciximab, eptifibatide, and heparin.

118. A method of treating psoriasis in a patient in need of such treatment, comprising administering to said patient a therapeutically effective amount of at least one compound of Claim 41, or a pharmaceutically acceptable salt or solvate thereof, in combination with at least one compound selected from the group consisting of immunosuppressives, steroids, and anti-TNF- $\alpha$  compounds.

119. A method of treating COPD in a patient in need of such treatment, comprising administering to said patient a therapeutically effective amount of at least one compound of Claim 41, or a pharmaceutically acceptable salt or solvate thereof.

120. A method of treating acute pain in a patient in need of such treatment, comprising administering to said patient a therapeutically effective amount of at least one compound of Claim 41, or a pharmaceutically acceptable salt or solvate thereof.

121. A method of treating acute inflammatory pain in a patient in need of such treatment, comprising administering to said patient a therapeutically effective amount of at least one compound of Claim 41, or a pharmaceutically acceptable salt or solvate thereof.

122. A method of treating chronic inflammatory pain in a patient in need of such treatment, comprising administering to said patient a therapeutically effective amount of at least one compound of Claim 41, or a pharmaceutically acceptable salt or solvate thereof.

123. A method of treating neuropathic pain in a patient in need of such treatment, comprising administering to said patient a therapeutically effective

amount of at least one compound of Claim 41, or a pharmaceutically acceptable salt or solvate thereof.

5 124. A method of treating arthritis in a patient in need of such treatment, comprising administering to said patient a thereapeutically effective amount of at least one compound of Claim 41, or a pharmaceutically acceptable salt or solvate thereof.

10 125. A method of treating osteoarthritis in a patient in need of such treatment, comprising administering to said patient a thereapeutically effective amount of at least one compound of Claim 41, or a pharmaceutically acceptable salt or solvate thereof.

126. The method of Claim 82 wherein said  
15 (a) Allograft rejections are selected from the group consisting of acute allograft rejections and chronic allograft rejections,  
(b) Early transplantation rejection is an acute allograft rejection,  
(c) Autoimmune deafness is Meniere's disease,  
(d) Myocarditis is viral myocarditis,  
(e) Neuropathies are selected from the group consisting of IgA  
20 neuropathy, membranous neuropathy and idiopathic neuropathy,  
(f) Autoimmune diseases are anemias, and  
(g) Vasculitis syndromes are selected from the group consisting of giant cell arteritis, Behcet's disease and Wegener's granulomatosis.

25 127. The method of Claim 108 wherein said  
(a) Allograft rejections are selected from the group consisting of acute allograft rejections and chronic allograft rejections,  
(b) Early transplantation rejection is an acute allograft rejection,  
(c) Autoimmune deafness is Meniere's disease,  
30 (d) Myocarditis is viral myocarditis,  
(e) Neuropathies are selected from the group consisting of IgA neuropathy, membranous neuropathy and idiopathic neuropathy,  
(f) Autoimmune diseases are anemias, and

(g) Vasculitis syndromes are selected from the group consisting of giant cell arteritis, Behcet's disease and Wegener's granulomatosis.

128. A method of treating a CXCR1 and/or a CXCR2 mediated disease or  
5 condition selected from the group consisting of: acute pain, acute inflammation,  
chronic inflammation, rheumatoid arthritis, acute inflammatory pain, chronic  
inflammatory pain, neuropathic pain, psoriasis, atopic dermatitis, asthma, COPD,  
adult respiratory disease, arthritis, inflammatory bowel disease, Crohn's disease,  
ulcerative colitis, septic shock, endotoxic shock, gram negative sepsis, toxic shock  
10 syndrome, stroke, cardiac reperfusion injury, renal reperfusion injury,  
glomerulonephritis, thrombosis, Alzheimer's disease, graft vs. host reaction, allograft  
rejections, malaria, acute respiratory distress syndrome, delayed type hypersensitivity  
reaction, atherosclerosis, cerebral ischemia, cardiac ischemia, osteoarthritis, multiple  
sclerosis, restinosis, angiogenesis, osteoporosis, gingivitis, respiratory viruses,  
15 herpes viruses, hepatitis viruses, HIV, Kaposi's sarcoma associated virus, meningitis,  
cystic fibrosis, pre-term labor, cough, pruritis, multi-organ dysfunction, trauma, strains,  
sprains, contusions, psoriatic arthritis, herpes, encephalitis, CNS vasculitis, traumatic  
brain injury, CNS tumors, subarachnoid hemorrhage, post surgical trauma, interstitial  
pneumonitis, hypersensitivity, crystal induced arthritis, acute pancreatitis, chronic  
20 pancreatitis, acute alcoholic hepatitis, necrotizing enterocolitis, chronic sinusitis,  
angiogenic ocular disease, ocular inflammation, retinopathy of prematurity, diabetic  
retinopathy, macular degeneration with the wet type preferred, corneal  
neovascularization, polymyositis, vasculitis, acne, gastric ulcers, duodenal ulcers,  
celiac disease, esophagitis, glossitis, airflow obstruction, airway  
25 hyperresponsiveness, bronchiectasis, bronchiolitis, bronchiolitis obliterans, chronic  
bronchitis, cor pulmonae, dyspnea, emphysema, hypercapnea, hyperinflation,  
hypoxemia, hyperoxia-induced inflammations, hypoxia, surgical lung volume  
reduction, pulmonary fibrosis, pulmonary hypertension, right ventricular hypertrophy,  
peritonitis associated with continuous ambulatory peritoneal dialysis (CAPD),  
30 granulocytic ehrlichiosis, sarcoidosis, small airway disease, ventilation-perfusion  
mismatching, wheeze, colds, gout, alcoholic liver disease, lupus, burn therapy,  
periodontitis, cancer, transplant reperfusion injury, and early transplantation rejection  
in a patient in need of such treatment comprising administering to said patient an

effective amount of at least one compound of Claim 1, or a pharmaceutically acceptable salt or solvate thereof.

129. A method of treating a CCR7 mediated disease or condition selected  
5 from the group consisting of: acute inflammation, chronic inflammation, acute  
inflammatory pain, acute pain, chronic inflammatory pain, neuropathic pain, acute  
allograft rejection, acute respiratory distress syndrome, adult respiratory disease,  
airway hyperreactivity, allergic contact dermatitis, allergic rhinitis, alopecia areata,  
alzheimer's disease, angiogenic ocular disease, antiphospholipid syndromes, aplastic  
10 anemia, asthma, atherosclerosis, atopic dermatitis, autoimmune deafness,  
autoimmune hemolytic syndromes, autoimmune hepatitis, autoimmune neuropathy,  
autoimmune ovarian failure, autoimmune orchitis, autoimmune thrombocytopenia,  
bronchiolitis, bronchiolitis obliterans syndrome, bullous pemphigoid, burn therapy,  
cancer, cerebral ischemia, cardiac ischemia, chronic allograft rejection, chronic  
15 allograft vasculopathy, chronic bronchitis, chronic inflammatory demyelinating  
polyneuropathy, chronic sinusitis, cirrhosis, CNS vasculitis, COPD, Cor pneumoniae,  
Crohn's disease, cryoglobulinemia, crystal-induced arthritis, delayed-type  
hypersensitivity reactions, dermatomyositis, diabetes, diabetic retinopathy, drug-  
induced autoimmunity, dyspnea, emphysema, epidermolysis bullosa acquisita,  
20 endometriosis, fibrotic diseases, gastritis, glomerulonephritis, Goodpasture's  
syndrome, graft vs host disease, Graves' disease, Guillain-Barre disease,  
Hashimoto's thyroiditis, hepatitis-associated autoimmunity, HIV-related autoimmune  
syndromes and hematologic disorders, hyperoxia-induced inflammation,  
hypercapnea, hyperinflation, hypophytis, hypoxia, idiopathic thrombocytic pupura,  
25 inflammatory bowel diseases, interstitial cystitis, interstitial pneumonitis, juvenile  
arthritis, Langerhans' cell histiocytitis, lichen planus, metal-induced autoimmunity,  
multiple sclerosis, myasthenia gravis, myelodysplastic syndromes, myocarditis  
including viral myocarditis, myositis, neuropathies, nephritic syndrome, ocular  
inflammation, optic neuritis, osteoarthritis, pancreatitis, paroxysmal nocturnal  
30 hemoglobinemia, pemphigus, polymyalgia, polymyositis, post-infectious  
autoimmunity, pulmonary fibrosis, primary biliary cirrhosis, psoriasis, pruritis,  
rheumatoid arthritis, reactive arthritis, ankylosing spondylitis, psoriatic arthritis,  
Raynaud's phenomenon, Reiter's syndrome, reperfusion injury, restenosis,  
sarcoidosis, scleritis, scleroderma, secondary hematologic manifestation of



autoimmune diseases, silicone implant associated autoimmune disease, Sjogren's syndrome, systemic lupus erythematosus, thrombocytopenia, thrombosis, transverse myelitis, tubulointerstitial nephritis, ulcerative colitis, uveitis, vasculitis and vasculitis syndromes, and vitiligo in a patient in need of such treatment comprising  
5 administering to said patient an effective amount of at least one compound of Claim 1, or a pharmaceutically acceptable salt or solvate thereof.

130. The method of Claim 128 wherein said

- 10 (a) Allograft rejections are selected from the group consisting of acute allograft rejections and chronic allograft rejections, and  
(b) Early transplantation rejection is an acute allograft rejection.

131. The method of Claim 129 wherein said

- 15 (a) Autoimmune deafness is Meniere's disease,  
(b) Myocarditis is viral myocarditis,  
(c) Neuropathies are selected from the group consisting of IgA neuropathy, membranous neuropathy and idiopathic neuropathy,  
(d) Autoimmune diseases are anemias, and  
20 (e) Vasculitis syndromes are selected from the group consisting of giant cell arteritis, Behcet's disease and Wegener's granulomatosis.